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Adapting Emergency Preparedness and Response Guidelines to the Digital Age CDS (Clinical Decision Support) Validation Report

Version 1.0

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Record of Changes

Version	Date	Author / Owner	Description of Change
1.0	October 17, 2018	CAMH Team	First draft submitted for sponsor review

Executive Summary

This report documents the validation of the Anthrax Post-Exposure Prophylaxis (PEP) Clinical Decision Support (CDS) developed for the Centers for Disease Control and Prevention (CDC) by CAMH. An overview of the validation of CDS in general is discussed, and a plan for validating the Anthrax PEP CDS is reviewed. The validation plan called for leveraging an open-source tool called Synthea™ for generating a set of representative synthetic patient records. The Anthrax PEP CDS was executed against these synthetic patient records, and the outputs were then evaluated by the CAMH clinical team, who were familiar with the CDC guidelines upon which the CDS is based. The overall findings of the synthetic patient testing were very good; only two of the test patients exhibited any issues with the CDS outputs, and said issues were resolvable through a bug fix in the software used to execute the CDS and not in the CDS itself. Finally, a number of key lessons learned are documented from the outcomes of the synthetic patient testing. To the extent within the limitations afforded by synthetic test data, the Anthrax PEP CDS has been validated using the procedures described in this report.

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1. Introduction

According to The Office of the National Coordinator for Health Information Technology [1]:

> *"Clinical decision support (CDS) provides clinicians, staff, patients or other individuals with knowledge and person-specific information, intelligently filtered or presented at appropriate times, to enhance health and health care. CDS encompasses a variety of tools to enhance decision-making in the clinical workflow. These tools include computerized alerts and reminders to care providers and patients; clinical guidelines; condition-specific order sets; focused patient data reports and summaries; documentation templates; diagnostic support, and contextually relevant reference information, among other tools."*

Clinical decision support, or CDS, represents a more efficient and consistent approach to distributing expert guidance in a manner that is less prone to transcription and interpretation errors compared to clinical guideline textual narrative alone. The Centers for Disease Control and Prevention (CDC) engaged the Centers for Medicaid & Medicare Services (CMS) Alliance to Modernize Healthcare (CAMH) Federally Funded Research and Development Center (FFRDC) to develop one CDS artifact[1] based upon a subset of the multiple anthrax guidelines published by the CDC. The CAMH FFRDC, sponsored by CMS and all divisions of the Department of Health and Human Services (HHS), is the first FFRDC dedicated to strengthening the nation's healthcare system. MITRE, an objective not-for-profit organization, operates CAMH in partnership with CMS and all HHS agencies to implement innovative ideas to solve our nation's toughest health problems.

The CDS artifact developed by CAMH focuses on post-exposure prophylaxis (PEP) [2] for adults exposed to anthrax. While the artifact is described in detail elsewhere [3], for the purposes of this report, it is helpful to know that the artifact provides recommendations for PEP treatment based upon the information found in the patient's electronic health record (EHR). Treatment can be in the form of a dose of the anthrax vaccine and/or a prescription for one of a number of recommended antimicrobial medications. Logic encoded into the CDS determines the patient-specific recommended treatment and can also provide a variety of alerts to the clinician under certain conditions (e.g., a documented patient allergy to one of the recommended treatments) [3].

The Anthrax PEP CDS artifact encapsulates the CDC guidance using modern health information technology (IT) standards and systems. In particular, it represents clinical information using standard codes and resources, such as the Logical Observation Identifiers Names and Codes (LOINC) system [4] for observations and measurements and the Fast Healthcare Interoperability Resources (FHIR) standard [5] for data formats and information exchange. The CDS artifact also aggregates certain clinical codes into value sets as appropriate, and these are posted on the Value Set Authority Center [6]. The deterministic and executable logic in the CDS artifact is implemented using the Clinical Quality Language (CQL) [7].

This report documents the testing and validation of the CDS artifact produced by CAMH for the Anthrax CDS project and is organized as follows. CDS validation in general is discussed in Section 2, as are the validation approach options that were considered for this effort. The CAMH

[1] A CDS artifact is an electronic document consisting of many formatted fields and related file attachments, which together describe the purpose and function of a specific CDS tool.

team and CDC jointly decided that a synthetic pilot was the most viable approach to validation of the anthrax CDS. Section 3 provides a description of the synthetic pilot plan, rationale, and methodology. A synthetic patient record generator, Synthea™, was leveraged to provide data for the pilot. Section 4 provides a description of Synthea™ as well as the modifications introduced to support the synthetic pilot. Section 5 provides an overview of the results from the synthetic pilot, with details listed in Appendix B. Lessons learned during the validation process are documented in Section 6. A conclusion section summarizes the key findings and results.

2. CDS Validation

If CDS does not represent the underlying clinical guidance in a precise and standard way, it will not be widely adopted and used. CDS validation is meant to ensure that a CDS truly represents the clinical recommendations and guidance upon which it is based. This section discusses CDS validation in general and the options considered for the anthrax CDS project.

2.1 Validation Purpose

CDS validation is generally not meant to imply validation of any underlying clinical guidance. Instead, the purpose of validation is to ensure that CDS reflects the intention of the underlying guidance in an accurate and unambiguous manner. Clinical guidelines can sometimes contain vague or ambiguous statements, frequently due to insufficient evidence for warranting additional specificity. A good CDS tool should accurately reflect the underlying guidance while also being precise and specific through the use of open standards and coding. A good CDS validation should not only verify that these criteria are met but should also provide insight into how the underlying guidelines could be made more precise and amenable to implementation as CDS.

2.2 Validation Components

CDS validation consists of several components, each of which addresses different aspects of CDS functionality. The first validation component starts with asking basic questions about the CDS, such as whether it makes use of valid and publicly available codes, value sets, clinical concepts, and data models. A CDS that only uses local and/or proprietary codes and data models is much less useful since it cannot be widely adopted without significant integration efforts. Another basic validation question is whether the CDS logic is written in an open, domain-specific, and platform-independent language, such as CQL [7]. CDS logic can be written in almost any programming language; however, CQL was designed for authoring CDS logic as well as Clinical Quality Measures (CQMs) and so can be considered particularly well suited here. Regardless of the implementing language, validation should ask whether the CDS logic can be readily converted to a machine-interpretable format (as is the case with CQL).

The second validation component consists of running a battery of internal or “built-in” tests, which ideally should have been written while the CDS was being developed. These built-in tests should test the full range of the CDS functionality and should verify that the CDS executes correctly when given the expected and well-formed data inputs. Sixty-one synthetic test patient records were defined during the development of the Anthrax PEP CQL [8]. These tests were created as part of a test-driven development (TDD) [9] approach to writing the Anthrax PEP CQL, where very short development/test cycles were repeated until the CDS was complete. These tests check a range of functionalities, including vaccine dose timing and trigger conditions for the alert messages produced by the CDS. While these built-in tests may contain edge-cases [10] (e.g., patients with missing or malformed data), generally they are closely aligned with what the CQL expects in terms of input data.

Pilot testing is the third validation component. During pilot testing, the CDS is exposed to a much wider variety of patient records to assess its robustness and completeness. While the built-in testing can and should be designed by the CQL developers as part of their TDD approach,

pilot testing should provide an independent avenue for assessing the CQL logic. In other words, pilot testing should afford the opportunity to ask whether assumptions made by the CQL logic about the data match reality. CDS validation pilots come in different types; the choice of what kind of pilot to use for a particular CDS is often framed as a "live versus synthetic" decision. However, as the next section discusses, the options are more nuanced than a binary decision.

2.3 Pilot Options

As shown in Figure 1, there are three dyadic choices to be made when designing a CDS validation pilot. The patient records can be from real patients or synthetically generated, the CDS can be executed live or in an offline (post facto) fashion, and the data can be from a real electronic health record (EHR) system or not. The three dyadic choices are discussed in more detail elsewhere [11]. The six viable options for a CDS validation pilot are shown in Figure 1.

Patient Type		Real		Synthetic	
CDS Execution		Live	Offline	Live	Offline
Data Source	EHR				
	Non-EHR				

Figure 1. CDS Validation Pilot Options

CAMH has previously delivered an Anthrax CDS Pilot Decision Briefing [11], which evaluated the six viable pilot options using a set of metrics. The conclusion reached in collaboration with CDC was that a synthetic, offline, non-EHR pilot was the option most likely to provide a useful validation, given the project budget and schedule constraints. The rationale for this decision included:

- Validation implementation does not require external collaborators.
- Open-source tools exist to generate synthetic data compatible with existing CAMH CQL capabilities.
- Synthetic data can be tailored for the anthrax use case addressed by the CDS.
- A variety of synthetic data can be generated to test CDS robustness and to model EHR idiosyncrasies.

After delivery of the Pilot Decision Briefing, CAMH formulated and executed a synthetic pilot plan. That plan is discussed in the next section.

3. Synthetic Pilot Plan

A synthetic pilot affords the opportunity to explore scenarios that would be difficult or impossible to realize in a live clinical setting. For the use case of interest to the Anthrax PEP CDS, EHR systems are not likely to have anthrax-related diagnoses due to the rare nature of the disease. Thus, a synthetic pilot can provide important lessons learned regarding preparation for a rapid response in an emergency situation. This section outlines the synthetic pilot plan for the Anthrax PEP CDS.

3.1 Overview

The synthetic pilot involves the generation of a set of synthetic patient records using an open-source tool called Synthea™, which is described in detail in Section 4. The Anthrax PEP CDS is then executed against the synthetic patient records using an open-source CQL execution framework [12] along with a library [13] for exposing FHIR patient bundles [14] to the CQL execution framework. For each synthetic patient record, the executed CDS outputs one of the following based upon the content of the patient record:

- Nothing
- An order set of recommended PEP treatments
- One or more alert messages
- Both an order set and one or more alerts

The outputs from the executed CDS are then evaluated by subject matter experts (SMEs) from the CAMH clinical team based on the underlying CDC guidelines. The evaluation by the clinical SME team forms the basis for the lessons learned documented in this report. In addition, the CDC solicited feedback from anthrax SMEs and external stakeholders for the Anthrax PEP CDS artifact [3] and implementation guide [8].

3.2 Methodology

Section 4 describes the synthetic patient records as well as the Synthea™ Anthrax model developed for this effort. One hundred test patient records[2] were generated with Synthea™, the records were executed against the CDS, and the CDS outputs were evaluated by the CAMH clinical SMEs. Figure 6 in Appendix A.1 shows a blank copy of the evaluation form used by the clinical SME team to assess the CDS outputs. The evaluation form consists of one row per synthetic patient record. For each patient, the clinical SME evaluator asked whether the CDS outputs are consistent with the content of the patient record. Two evaluators were used for the first 10 synthetic patient records, and the remaining records were reviewed by just one evaluator. Any inconsistencies found in the remaining records were reviewed by both evaluators, and then confirmed with the CAMH pilot team.

While the outputs of the CDS are described elsewhere [8], for reference a summary has been included below in Table 1. Six CDS outputs are potential alert messages, and one output is the

[2] Because Synthea™ allows for patients to die, 112 test patients (100 living) ended up being generated and processed by the CDS.

order set of recommended PEP treatments. The CDS output names in Table 1 are written in camel case [15] because that is the naming convention used by the CQL for the Anthrax PEP CDS. Each of the CDS outputs is formatted as particular a type of FHIR Second Draft Standard for Trial Use (DSTU2) [16] or Third Standard for Trial Use (STU3) [17] resource.

Table 1. Summary of Anthrax PEP CDS Outputs

CDS Output	FHIR Resource Type	Description
FlagNoAsymptomaticObservation	Flag (DSTU2)	Patient is exposed to anthrax but does not have an asymptomatic Observation. If this is the case, a Flag resource will be generated below to highlight this issue, since post exposure prophylaxis is only recommended for asymptomatic patients. If the patient is both exposed and asymptomatic, then this Flag resource will be empty.
DetectedIssueExistingAntimicrobialRx	DetectedIssue (DSTU2)	Patient has at least one existing prescription to one of the recommended antimicrobials. If the patient is exposed, asymptomatic, and has an active Rx for a pertinent antimicrobial, a DetectedIssue resource will be generated which will reference the most recent Medication resource for one of the antimicrobials. If the patient does not have an existing Rx, then this DetectedIssue resource will be empty.
FlagAntimicrobialMedicationAllergies	Flag (DSTU2)	Patient potentially has an allergy to one of the antimicrobials. If the patient is exposed, asymptomatic, and has an AllergyIntolerance resource for one of the recommended antimicrobials, a Flag resource will be generated to alert on this. If the patient has no allergies, then this Flag resource will be empty.
FlagBioThraxAllergy	Flag (DSTU2)	Patient potentially has an allergy to the anthrax vaccine. If the patient is exposed, asymptomatic, and has an AllergyIntolerance resource for the anthrax vaccine, a Flag resource will be generated to alert on this. If the patient has no allergies to the vaccine, then this Flag resource will be empty.
FlagLatexAllergy	Flag (DSTU2)	Patient potentially has an allergy to latex. If the patient is exposed, asymptomatic, and has resources indicating an allergy to latex, a Flag resource will be generated to alert on this. If the patient has no allergies to latex, then this Flag resource will be empty.
DetectedIssueBioThraxHistoryInconsistencies	DetectedIssue (DSTU2)	Patient BioThrax dosing history has data consistency issues. Either there is an indication that the recommended dosing sequence was not followed (i.e., there is a missing dose), or the last vaccine Procedure is missing a date. Under these conditions, this CDS cannot reliably provide the correct PEP treatment recommendations. If there is a missing dose in the vaccine sequence, or if the last vaccine Procedure is missing a date, then a DetectedIssue resource will be generated which will reference the most recent vaccine Procedure resource. If no inconsistencies are found, then this DetectedIssue resource will be empty.
OrderSet	PlanDefinition (STU3)	The order set containing the recommended treatment for Anthrax PEP. It references the ActionList and the ContainedResourcesList, which contain the recommended treatments, possibly including an antimicrobial prescription and/or a vaccine dose. If treatment is not recommended, then this resource will be empty.

The SME evaluators first reviewed a synthetic patient record, and then examined the corresponding CDS outputs and compared that against the intended output. If an output was

correctly populated, then the evaluators marked that entry in the form shown in Appendix A.1 with a "1" as an indication of correctness. Otherwise, the evaluators left the "0" value in that entry of the evaluation form to designate an incorrect response. The evaluation form also contains a column for the evaluators to record comments regarding errors in the outputs. The results from this evaluation are discussed in Section 5.

In addition to the evaluation by the CAMH clinical SMEs, a questionnaire was prepared for CDC to solicit feedback on the Anthrax PEP CDS. The questionnaire is shown in Figure 7 in Appendix A.2.

3.3 Discussion

As discussed in Section 2.2, CDS validation consists of several components. There are similarities between the "built-in" tests and the synthetic patient records referenced above. However, there are several important differences between the two, which are described in more detail below.

The built-in testing that should accompany the CQL development is what is referred to in software development as clear-box testing [18]. These tests are designed with a knowledge of how the CQL operates (i.e., they can see inside the "box" being tested). In other words, the tests and the CQL are tailored for each other. Especially if a TDD approach is being taken with the CQL development, the built-in tests should pass by definition [9].

In contrast, the pilot synthetic test patients use very little information about how the CQL functions. This means that the synthetic pilot is a form of what is referred to in software development as black-box testing [19]. Having an independent tool like Synthea™ generate synthetic test patient records makes the validation more robust and complete.

The format of the patient records generated by Synthea™ may contain syntactic differences due to variations sometimes seen with FHIR export implementations. Put another way, the synthetic patient records generated using Synthea™ could be expected to have slight differences compared to those produced for the built-in testing. In addition, Synthea™ generates pseudorandom [20] patient records, which will help to evaluate unanticipated edge cases [10]. Having a clinical SME assess a modest number of black-box test records, along with the output from the CDS, provides additional insights and validation.

A sample size of 100 records was chosen for the synthetic pilot based upon the number of parameters of the Anthrax population model (see Section 4.2) and the number of CDS output combinations.[3] Additional synthetic test patient records could have been generated; however, they would most likely be redundant and not test a new or unique clinical scenario. The CDS outputs were evaluated manually by necessity since the randomness of Synthea™ ensures that there is not an answer key. Increasing the size of the synthetic pilot would greatly increase the amount of effort on the part of the clinical SMEs doing the evaluation, and likely provide little additional benefit. While not strictly appropriate here, cursory sample size calculations appear to support this claim [21].

[3] There are 27 possible values for OrderSet plus the six potential alerts listed in Table 1.

4. Synthetic Patient Record Generation

A key component of the synthetic pilot is the synthetic patient records used as data inputs for the Anthrax PEP CDS. These records are created using the Synthea™ open-source synthetic patient generator [22]. This section describes Synthea™, Synthea's Generic Module Framework (GMF) for modeling diseases and treatment, and the anthrax module developed in support of the synthetic pilot.

4.1 Synthea™

Synthea™ is an open-source tool for generating synthetic patient records [22]. The goal of Synthea™ is to provide statistically and demographically accurate patient medical history records that are free from cost, privacy, and security concerns. The medical history records generated by Synthea™ are not real but instead are synthetically generated using models informed by publicly available databases for population demographics, provider information, and healthcare costs [23].

4.1.1 Overview

A high-level depiction of the Synthea™ architecture is shown below in Figure 2. Synthea™ is written in the Java programming language [24] and takes an agent-based approach [25] to generating synthetic patient records. Each synthetic patient in the population independently progresses from birth to the current date (or death, whichever comes first). Random models called modules are applied to each synthetic patient to account for diseases and clinical encounters. Once all synthetic patients are either updated to the current date or are deceased, the records can be output in a number of formats [26].

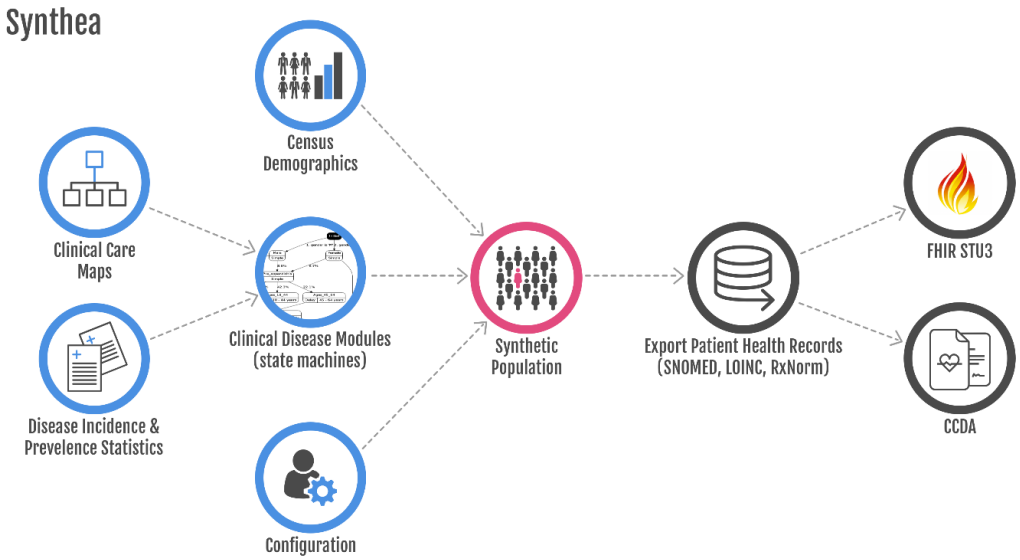


Figure 2. Synthea™ Architecture
Source: https://github.com/synthetichealth/synthea/wiki/Getting-Started

4.1.2 Modules

Synthea™ provides a GMF for defining random models of diseases and clinical treatments and encounters [27]. Referred to as clinical disease modules or simply "modules," these random models are written in JavaScript Object Notation (JSON), a common format for defining and exchanging structured data [28]. Each module is written for a specific type of disease or treatment and consists of a number of states and state transition probabilities. The synthetic patients in the population randomly traverse through the states in each module as the simulation time progresses. Transition from one state in a module to another can be deterministic [29] or random, and is influenced by the specified state transition probabilities and other control mechanisms such as guards [30]. An example state diagram from the Synthea™ documentation is reproduced below in Figure 3.

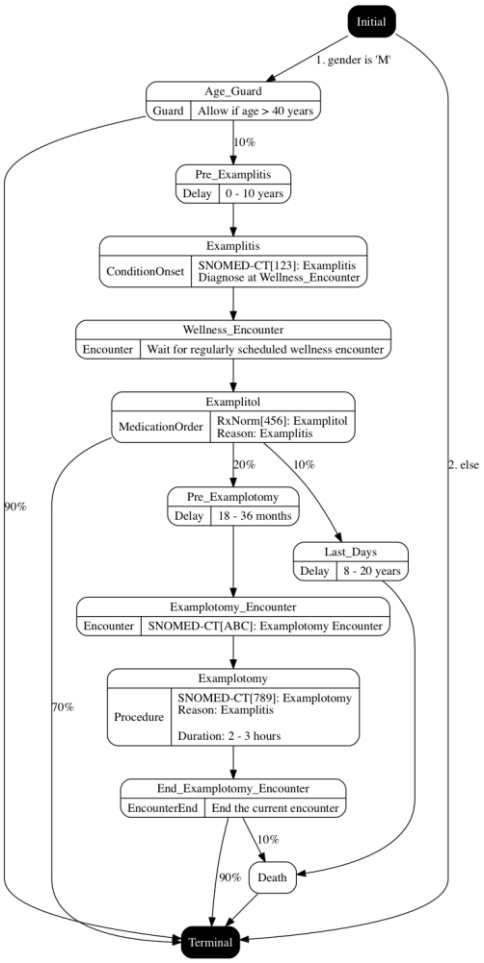


Figure 3. State Diagram for an Example Synthea™ Module
Source: https://github.com/synthetichealth/synthea/wiki/Generic-Module-Framework%3A-Complete-Example

As can be seen in Figure 3, Synthea's GMF allows detailed models to be built up that can describe the nature and timing of diseases, treatments, and encounters. Synthea™ comes with a growing set of modules, including models for the top 10 reasons patients visit a primary care physician and the top 10 conditions in terms of years of life lost [31]. As will be described later in this report, a Synthea™ module for describing anthrax exposure and treatment was developed to support this pilot.

4.1.3 Export

Synthea™ allows synthetic patient records to be output to various file formats. Two formats are critical for the synthetic pilot: FHIR DSTU2 and text. The first format allows the synthetic patient records to be output as a FHIR DSTU2 patient bundle in a JSON format. This format is important because it is the one the CQL execution framework ingests and processes due to the use of the FHIR data source library [13]. If Synthea™ had not been able to output in FHIR DSTU2 format, then a translator would have to have been written. The second format exports the patient records in a simple and human-readable plain text. When the text format is used, much of

the coding and extraneous structure in the records is removed, making it easier for humans to interpret. The clinical SME evaluators use this plain text format as they assess each test patient in the pilot. An example of this simple format is provided later in this section (see Figure 5).

4.1.4 Modifications

Synthea™ is still under active development, and contributors regularly add new features [32]. Examples of new capabilities include additional modules for a greater number and variety of diseases, as well as an expanded ability to control the configuration and timing within the modules. For this pilot, a custom anthrax module was developed because no such model existed in Synthea's current library; that module is described in the next section. The remainder of this section describes other changes made to the Synthea™ codebase by the Anthrax CDS team in order to execute the pilot.

The changes made to the Synthea™ codebase only impacted behavior of the software during patient record export. Specifically, the changes were made to the FHIR DSTU2 export capability. The reason the changes were made was to relax assumptions made by Synthea™ regarding how the fields of certain FHIR DSTU2 resources were populated.

FHIR DSTU2 Observation resources are meant to capture "measurements and simple assertions made about a patient" [33]. The Anthrax PEP CDS assumes that exposure to anthrax, asymptomatic findings, and pregnancy observations can all be represented as different codes in a FHIR DSTU2 Observation resource [8]. However, Synthea™ only allows Observations to have one specific type of code system (LOINC). A modification was introduced to Synthea™ to allow other types of code systems to be used (e.g., SNOMED-CT [34]). Without this modification, Synthea™ could potentially produce FHIR DSTU2 Observation resources with the incorrect code system, which would result in the resource not being correctly filtered due to a code / code system mismatch.

FHIR DSTU2 AllergyIntolerances [35] are meant to document "risk of harmful or undesirable, physiological response which is unique to an individual and associated with exposure to a substance." The Anthrax PEP CDS assumes that pertinent allergies and intolerances are represented as different codes in a FHIR DSTU2 AllergyIntolerance resource [8]. The Synthea™ FHIR DSTU2 exporter assumes that codes within all AllergyIntolerance resources are in the SNOMED-CT code system [34]. This is not the case when RxNorm codes [36] are used to represent substances to which a patient may be allergic. A modification was introduced to Synthea™ to allow other types of code systems to be used in FHIR DSTU2 AllergyIntolerance resources. Without this modification, Synthea™ could potentially produce FHIR DSTU2 AllergyIntolerance resources with the incorrect code system, which would result in the resource not being correctly filtered due to a code / code system mismatch.

4.2 Anthrax Module

A Synthea™ module was developed in support of this pilot to allow for the anthrax exposure and treatment cycle to be modeled at a level appropriate for the CDS. The anthrax module is based upon the CDC guidelines, the Anthrax PEP CDS, and feedback from the CDC Anthrax SMEs. As with other Clinical Disease Modules included with Synthea™, the anthrax module is a pseudo-random state transition diagram. A visualization of the module rendered using the open-

source Graphviz tool [37] is shown below in Figure 4, while the following paragraphs describe the different aspects of the model.

The anthrax module consists of four sections:

- Allergies
- Exposure and initial visit
- Antimicrobial treatment
- Vaccine administration

The allergies section is visible in the bottom-right portion of Figure 4. A simple probability distribution and pseudo-random number generator are used to determine if a patient has allergies to any of the recommended PEP treatments. The allergy transition probabilities are configurable parameters of the module, and the values used in the pilot are shown in Table 2.

The initial anthrax exposure and initial visit are modeled as a random distribution spanning day 220 through day 250 of 2018. All patients leaving the allergies section enter the exposure and initial visit section. Exposure and initial visit are grouped together due to a limitation in Synthea™ where guard nodes [30], which are used to tell a module to wait until a certain condition is met, can only specify the year of exposure, and not any finer date or time granularity. The random delay of 220 through 250 days is used to force Synthea™ to output records close to the actual time of the synthetic pilot (i.e., late August and early September 2018). This random delay is a configurable parameter of the module, as are the proportion of synthetic patients being exposed to anthrax and those who are asymptomatic. The values used for these parameters are listed below in Table 2.

Patients who are randomly selected as not being exposed proceed directly to the terminal state of the module (shown as the black leftmost node in Figure 4) and remain there until the end of the simulation. All other patients proceed to the antimicrobial treatment section. The fraction of patients randomly receiving a type of antimicrobial treatment is controlled by the parameters listed in Table 2. Patients also have a chance at entering the vaccine administration section, where the timing between doses is random and controlled by additional configuration parameters. Table 2 provides a concise summary of these parameters, and the complexity of the model provides for the ability to consider a range of scenarios. Clinical scenario evaluation is outside the scope of this report.

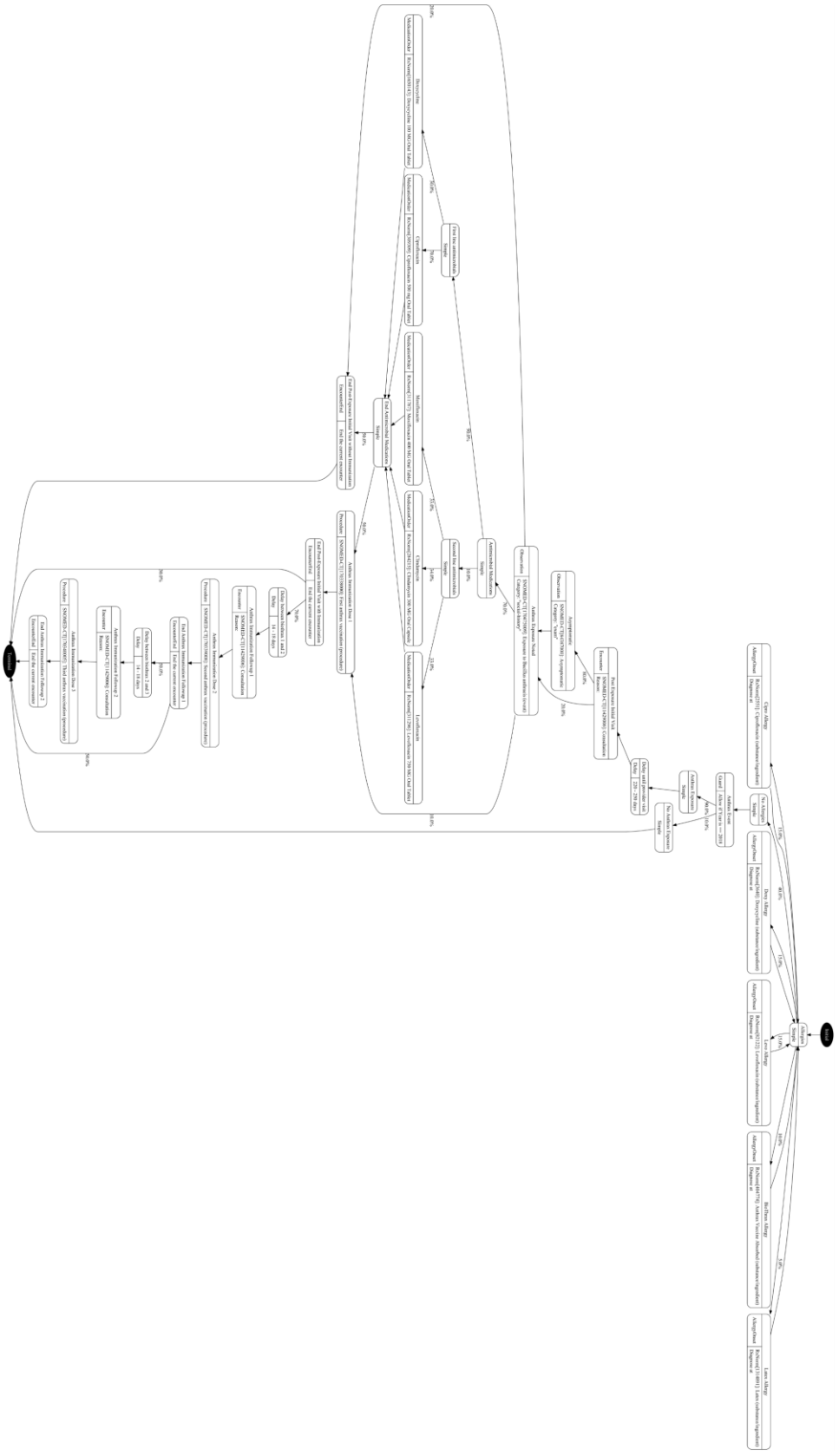


Figure 4. Graphviz Rendering of Anthrax Synthea™ Module

Table 2. List of Anthrax Synthea™ Module Parameters

Anthrax Module Parameter	Value Used In Pilot	
Year of anthrax event	2018	
Delay into year of initial provider visit	Uniform random distribution: 220-250 days	
Probability of patient being exposed to anthrax	0.90	
Probability for exposed patient to be asymptomatic	0.80	
Probability for patient to have no allergies	0.40	Must sum to 1.0
Allergy transition probability: ciprofloxacin allergy	0.15	
Allergy transition probability: doxycycline allergy	0.15	
Allergy transition probability: levofloxacin allergy	0.15	
Allergy transition probability: BioThrax® allergy	0.10	
Allergy transition probability: latex allergy	0.5	
Probability for exposed patient to receive no treatment on initial visit	0.20	Must sum to 1.0
Probability for exposed patient to only receive the first BioThrax® dose	0.10	
Probability for exposed patient to receive an antimicrobial and possibly the first BioThrax® dose	0.70	
Probability for patient receiving an antimicrobial to receive a first-line antimicrobial	0.90	Must sum to 1.0
Probability for patient receiving an antimicrobial to receive a second-line antimicrobial	0.10	
Probability for patient receiving a first-line antimicrobial to receive ciprofloxacin	0.70	Must sum to 1.0
Probability for patient receiving a first-line antimicrobial to receive doxycycline	0.30	
Probability for patient receiving a second-line antimicrobial to receive moxifloxacin	0.33	Must sum to 1.0
Probability for patient receiving a second-line antimicrobial to receive clindamycin	0.34	
Probability for patient receiving a second-line antimicrobial to receive levofloxacin	0.33	
Probability for patient receiving an antimicrobial to also receive the first BioThrax® dose	0.50	Must sum to 1.0
Probability for patient receiving an antimicrobial to not receive first BioThrax® dose	0.50	
Probability for patient receiving the first BioThrax® dose to go on to receive the second dose	0.70	Must sum to 1.0
Probability for patient receiving the first BioThrax® dose to not go on to receive the second dose	0.30	
Delay between BioThrax® doses 1 and 2	Uniform random distribution: 14-18 days	
Probability for patient receiving the second BioThrax® dose to go on to receive the third dose	0.5	Must sum to 1.0
Probability for patient receiving the second BioThrax® dose to not go on to receive the third dose	0.5	
Delay between BioThrax® doses 2 and 3	Uniform random distribution: 14-18 days	

4.3 Example Record

As mentioned in Section 4.1.3, the synthetic patient records can be output in several different formats. The plain text format is useful for the pilot since it is human readable and thus easily interpreted by the clinical SME evaluators. An example of the one of the pilot records is provided below in Figure 5. It contains information derived from all the modules in Synthea™, including the anthrax module. The inclusion of non-anthrax-related information is one of the aspects of the synthetic pilot that provides for a more realistic testing environment.

```
Esther279 Kassulke119
=====================
Race:                Native
Ethnicity:           Non-Hispanic
Gender:              F
Age:                 19
Birth Date:          1998-10-02
Marital Status:      S
Outpatient Provider: BARTLETT REGIONAL HOSPITAL
--------------------------------------------------------------------------------
ALLERGIES:
2018-08-21 -            : Levofloxacin (substance/ingredient)
2018-08-21 -            : Anthrax Vaccine Absorbed (substance/ingredient)
--------------------------------------------------------------------------------
MEDICATIONS:
2018-08-28[CURRENT] : Yaz 28 Day Pack
2018-08-21[CURRENT] : Ciprofloxacin 500 mg Oral Tablet
2016-09-07[STOPPED] : Nexplanon 68 MG Drug Implant
2015-12-09[STOPPED] : Amoxicillin 250 MG / Clavulanate 125 MG [Augmentin] for Viral
                      sinusitis (disorder)
2015-09-13[STOPPED] : Seasonique 91 Day Pack
2013-09-23[STOPPED] : Levora 0.15/30 28 Day Pack
2013-09-14[STOPPED] : Acetaminophen 160 MG for Acute bronchitis (disorder)
--------------------------------------------------------------------------------
CONDITIONS:
2015-12-09 - 2015-12-16 : Viral sinusitis (disorder)
2013-09-14 - 2013-09-28 : Acute bronchitis (disorder)
2011-02-20 - 2011-02-27 : Viral sinusitis (disorder)
2008-12-17 - 2008-12-24 : Viral sinusitis (disorder)
--------------------------------------------------------------------------------
CARE PLANS:
2013-09-14[STOPPED] : Respiratory therapy
                        Reason: Acute bronchitis (disorder)
                        Activity: Recommendation to avoid exercise
                        Activity: Deep breathing and coughing exercises
--------------------------------------------------------------------------------
OBSERVATIONS:
2018-08-21 : Exposure to Bacillus anthracis (event)   1.0
2018-08-21 : Asymptomatic                             1.0
2017-12-01 : Blood Pressure
           - Diastolic Blood Pressure                 73.8 mmHg
           - Systolic Blood Pressure                  114.1 mmHg
2017-12-01 : Body Mass Index                          21.9 kg/m2
2017-12-01 : Body Weight                              64.2 kg
2017-12-01 : Body Height                              171.4 cm
2016-11-25 : Blood Pressure
           - Diastolic Blood Pressure                 88.1 mmHg
           - Systolic Blood Pressure                  136.7 mmHg
<-------------- ADDITIONAL RECORDS REMOVED FOR DISPLAY PURPOSES. -------------->
2008-10-10 : Body Mass Index                          17.4 kg/m2
2008-10-10 : Body Weight                              37.6 kg
2008-10-10 : Body Height                              146.9 cm
--------------------------------------------------------------------------------
PROCEDURES:
2016-09-07 : Insertion of subcutaneous contraceptive
2014-11-14 : Documentation of current medications
2013-11-08 : Documentation of current medications
2011-10-28 : Documentation of current medications
2008-10-10 : Documentation of current medications
--------------------------------------------------------------------------------
IMMUNIZATIONS:
2017-12-01 : Influenza, seasonal, injectable, preservative free
2016-11-25 : Influenza, seasonal, injectable, preservative free
2015-11-20 : Influenza, seasonal, injectable, preservative free
2014-11-14 : meningococcal MCV4P
<-------------- ADDITIONAL RECORDS REMOVED FOR DISPLAY PURPOSES. -------------->
2009-10-16 : Tdap
2008-10-10 : Influenza, seasonal, injectable, preservative free
--------------------------------------------------------------------------------
ENCOUNTERS:
2018-08-28 : Consultation for treatment
2018-08-21 : Consultation
2017-12-01 : Encounter for check up (procedure)
<-------------- ADDITIONAL RECORDS REMOVED FOR DISPLAY PURPOSES. -------------->
2008-12-17 : Encounter for Viral sinusitis (disorder)
2008-10-10 : Encounter for check up (procedure)
--------------------------------------------------------------------------------
IMAGING STUDIES:
--------------------------------------------------------------------------------
```

Figure 5. Example Synthetic Patient Record in Text Format

5. Synthetic Pilot Outcomes

This section describes the outcomes from the synthetic pilot described in Section 3. This synthetic pilot serves as a validation of the Anthrax PEP CDS, within the limitations afforded by purely synthetic testing. The results of the pilot are discussed in this section, as are the issues identified during the evaluation.

5.1 Evaluation Results

Table 3 below summarizes the results from the 112 test patients (12 deceased and 100 living) generated using Synthea™ with the anthrax module. Out of the 112 test patients, just two had identified issues, both of which were resolvable. The issue that impacted the two patient records is discussed in the next section, while detailed patient results are listed in Appendix B.

Table 3. Summary of Results from Synthetic Pilot

Total Number of Synthetic Patients	Number of Synthetic Patients with No Issues	Number of Synthetic Patients with Resolvable Issues	Number of Synthetic Patients with Unresolvable Issues
112	110	2	0

Figure 8 through Figure 17 in Appendix B list the evaluation results for each test patient, as entered by the CAMH clinical SME team. Issues are indicated by a "0" in the corresponding cell of the evaluation spreadsheet. These cells are also color-coded red to highlight the issues. Comments appear next to entries with identified issues but can also appear next to other test patients (e.g., Patient 61 in Figure 12). The appearance of a comment does not necessarily indicate that any issues have been identified for a test patient.

5.2 Addressed Issues

Patients 1 (Figure 8) and 85 (Figure 15) both were determined by the clinical SME evaluators to have been incorrectly given an order set recommending a dose of the anthrax vaccine despite the fact that only 13 days had elapsed since the last dose.[4] Review of the CQL vaccine timing logic and associated built-in tests confirmed that the CDS appeared to be correctly specifying a 14-day spacing between vaccine doses. Upon further investigation, a time zone bug was discovered in the CQL execution framework used to run the CDS. The synthetic patient records were generated assuming a certain time zone (Eastern Daylight Time), but a different time zone (Eastern Standard Time) was assumed when evaluating the CDS using the CQL execution framework.

The CQL execution framework has logic that is meant to account for time zone differences when comparing two dates; however, there is a bug in the logic. The CDS specifies a required difference in time to be 14 days, which according to the CQL standard [7] implies a certain resolution whereby small-time differences (i.e., hours, minutes, seconds) should be ignored when comparing two dates. This is exactly what the CQL execution framework attempts to do; however, it discards the small-time differences prior to the time zone adjustment. This results in

[4] The CDS should only recommended another vaccine dose if 14 days have elapsed since the last dose.

the issue observed with Patients 1 and 85, where only 13 calendar days had elapsed since the last vaccine dose but the CQL execution framework was calculating a 14-day difference, which triggered the next dose in the CDS vaccine logic.

Since the CDS vaccine logic is indeed correct, fixing the bug in the CQL execution framework resulted in the correct order set being output by the CDS for Patients 1 and 85. However, the results in this report were purposefully not updated to reflect the occurrence of this [resolvable] issue. The bug was only fixed in a local copy of the CQL execution framework; however, it was discovered that others fixed this bug in the main repository shortly after the synthetic pilot was completed [38].

5.3 Discussion

Given the complexity of the anthrax module, the variety of the synthetic patient data, and the number of test patients, the Anthrax PEP CDS performed remarkably well. Only a single issue was identified, which impacted only two (2%) of the 112 patient records in the test sample. This issue was not directly related to the CQL but instead to the open-source tool for executing the CQL. Fixing the bug in the open-source tool resolved the issue. No unresolvable issues were encountered during the evaluation.

6. Lessons Learned

Multiple lessons were learned during the synthetic pilot and associated validation activities. This section documents these lessons learned and describes how they can improve the CDS development and validation process in the future.

6.1 Test-Driven Development

As described in Section 2.2, a TDD approach was taken while the Anthrax PEP CQL was being written. This means that desired CDS functionality was first described in an automated test, and then just enough CQL was written to ensure the test passed. One of the benefits of TDD is that the resulting code tends to have fewer defects and bugs compared to software written using other approaches [9]. One lesson learned from this synthetic pilot is that the very small number of [resolvable] issues is likely due to the TDD approach used to write the CQL.

6.2 Understand Synthetic Data Assumptions

As described in Section 4.1.4, some changes had to be made to Synthea™ before it could be used to generate appropriate data for this pilot. This was because Synthea™ made several narrow assumptions about what code systems could be used in FHIR DSTU2 resources. Preparation for the synthetic pilot afforded the opportunity to understand the assumptions and restrictions made by the tool used to generate the synthetic test patient data. Understanding these limitations was key to designing an appropriate synthetic pilot for the validation of the Anthrax PEP CDS.

6.3 Error Tracing

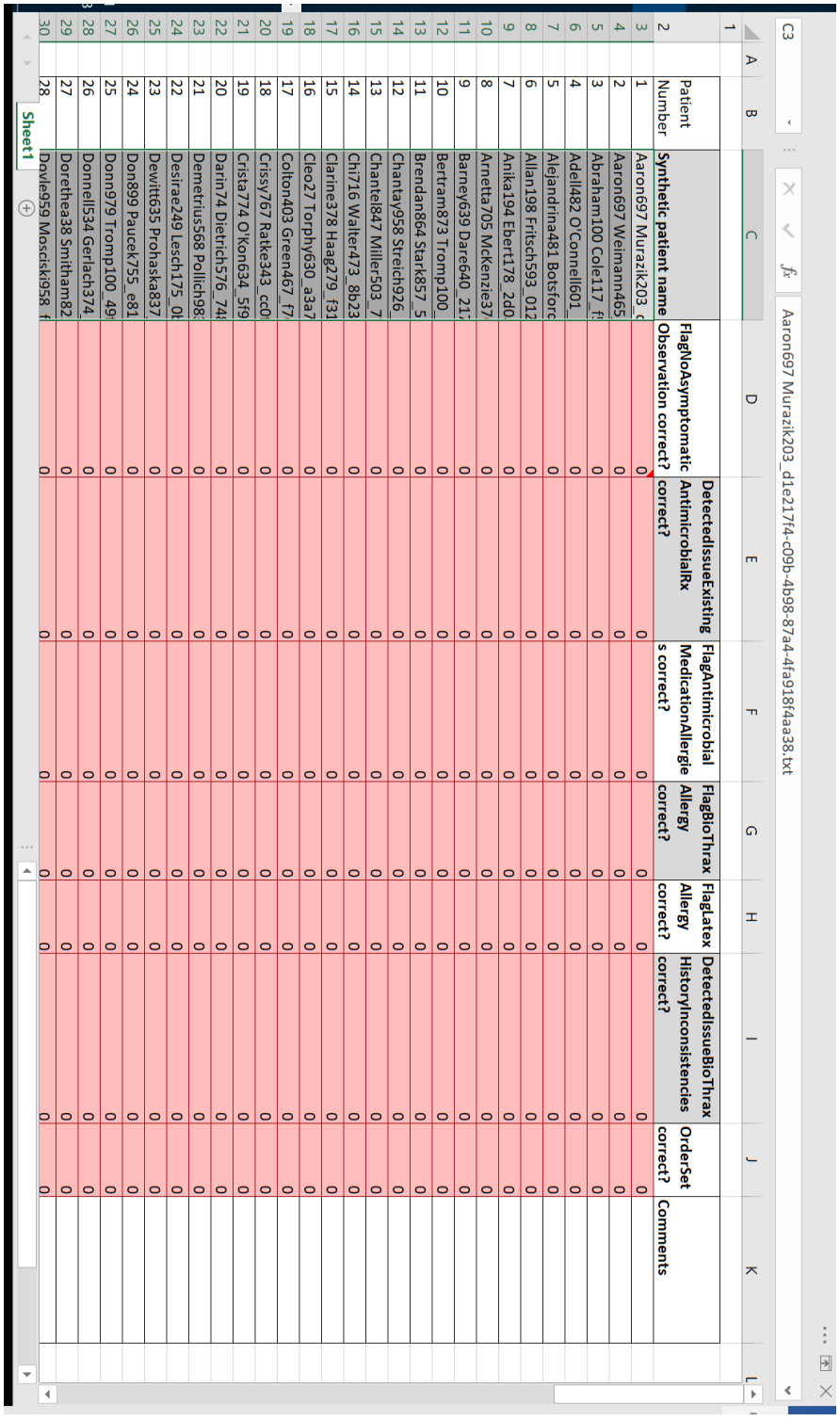
As described in Section 5.2, an issue was found with two of the synthetic test patients. Having the ability to debug and trace the error to the CQL execution framework was critical to resolving this issue. If a robust debugging capability had not been in place, then resolving this issue might have not been possible. This serves as another lesson learned when piloting and validating CDS.

7. Conclusion

This report has documented the validation of the Anthrax PEP CDS. Validation of CDS was discussed, and a plan for validating the Anthrax PEP CDS was reviewed. The synthetic pilot plan leveraged an open-source tool, Synthea™, for generating a set of synthetic patient records. The Anthrax PEP CDS was executed against these synthetic patient records, and the outputs were evaluated by the CAMH clinical SME team. The overall findings of the synthetic pilot were very good; only two test patients exhibited issues during the evaluation. One software bug was identified as causing both patient issues, which was resolved through a fix in the software used to execute the CDS. Finally, key lessons learned from the outcomes of the synthetic pilot were documented. Within the limitations afforded by synthetic patient records test data, the Anthrax PEP CDS has been validated using the procedures described in this report.

Appendix A. Evaluation Resources

A.1 Synthetic Pilot Evaluation Spreadsheet



Patient Number	Synthetic patient name	FlagNoAsymptomatic Observation correct?	DetectedIssueExisting AntimicrobialRx correct?	FlagAntimicrobial MedicationAllergies correct?	FlagBioThrax Allergy correct?	FlagLatex Allergy correct?	DetectedIssueBioThrax HistoryInconsistencies correct?	OrderSet correct?	Comments
1	Aaron697 Murazik203_	0	0	0	0	0	0	0	
2	Aaron697 Weimann465	0	0	0	0	0	0	0	
3	Abraham100 Cole117_F	0	0	0	0	0	0	0	
4	Adell482 O'Connell601_	0	0	0	0	0	0	0	
5	Alejandrina481 Botsforc	0	0	0	0	0	0	0	
6	Allan198 Fritsch593_012	0	0	0	0	0	0	0	
7	Anika194 Ebert178_2d0	0	0	0	0	0	0	0	
8	Arnetta705 Mckenzie37	0	0	0	0	0	0	0	
9	Barney639 Dare640_217	0	0	0	0	0	0	0	
10	Bertram873 Tromp100_	0	0	0	0	0	0	0	
11	Brendan864 Stark857_5	0	0	0	0	0	0	0	
12	Chantay958 Streich926_	0	0	0	0	0	0	0	
13	Chantel847 Miller503_7	0	0	0	0	0	0	0	
14	Chi716 Walter473_8b23	0	0	0	0	0	0	0	
15	Clarine378 Haag279_f31	0	0	0	0	0	0	0	
16	Cleo27 Torphy630_a3a7	0	0	0	0	0	0	0	
17	Colton403 Green467_f7	0	0	0	0	0	0	0	
18	Crissy767 Ratke343_cc0	0	0	0	0	0	0	0	
19	Crista774 O'Kon634_5f9	0	0	0	0	0	0	0	
20	Darin74 Dietrich576_744	0	0	0	0	0	0	0	
21	Demetrius568 Pollich98	0	0	0	0	0	0	0	
22	Desirae249 Lesch175_0t	0	0	0	0	0	0	0	
23	Dewitt635 Prohaska837	0	0	0	0	0	0	0	
24	Don899 Paucek755_e81	0	0	0	0	0	0	0	
25	Donn979 Tromp100_49f	0	0	0	0	0	0	0	
26	Donnell534 Gerlach374_	0	0	0	0	0	0	0	
27	Dorethea38 Smitham82	0	0	0	0	0	0	0	
28	Doyle959 Mosciski858_f	0	0	0	0	0	0	0	

Figure 6. Synthetic Pilot Evaluation Spreadsheet (Blank)

A.2 CDS Artifact Questionnaire

Evaluation Questionnaire: Anthrax CDS Artifact

Purpose: This questionnaire accompanies the anthrax clinical decision support (CDS) artifact and supporting documentation. The goal of this questionnaire is to gather feedback regarding the utility of the artifact and clarity of supporting documentation.

General Questions:

1. Are the following clearly and consistently communicated throughout the CDS and documentation?
   - Goal(s) and rationale for CDS — Yes☐ No☐
   - Supporting clinical evidence and guidelines — Yes☐ No☐
   - Assumptions made by the CDS — Yes☐ No☐
2. Is the scope of the CDS appropriate for its application? Yes☐ No☐
3. Do you have any general feedback on the quality and/or formatting of the CDS, the supporting materials, or documentation?
   Click or tap here to enter text.

Clinical Questions:

4. Do you have any specific feedback regarding how allergies are represented in the CDS?
   Click or tap here to enter text.
5. Do you have any specific feedback regarding how immunizations are represented in the CDS?
   Click or tap here to enter text.
6. Do you have any general feedback on the value sets, codes and/or code systems used by the CDS?
   Click or tap here to enter text.
7. Is it clear how the CDS would fit into a clinical workflow? Yes☐ No☐
8. Are the CDS triggers clearly documented and sensible? Yes☐ No☐
9. For communicating messages to clinicians, such as for allergies, do you use default messages or custom messages tailored for CDS?
   Default☐ Custom☐
10. How do you calculate durations (e.g., between vaccines, from an exposure to the date of a visit)?
    Click or tap here to enter text.

Clinical Quality Language (CQL) Logic Questions:

11. Is the CQL clearly written and sufficiently documented? Yes☐ No☐
12. Is the complexity of the CDS appropriate for its application? Yes☐ No☐
13. Do you feel that the CQL correctly implements the semi-structured (L2) description of the CDS? Yes☐ No☐
14. Do you have any comments or concerns regarding the alerts or order sets produced by the CQL?
    Click or tap here to enter text.
15. Do you have any specific feedback on the data model and FHIR resources used by the CQL?
    Click or tap here to enter text.
16. Do you have any suggestions for improving the CQL?
    Click or tap here to enter text.

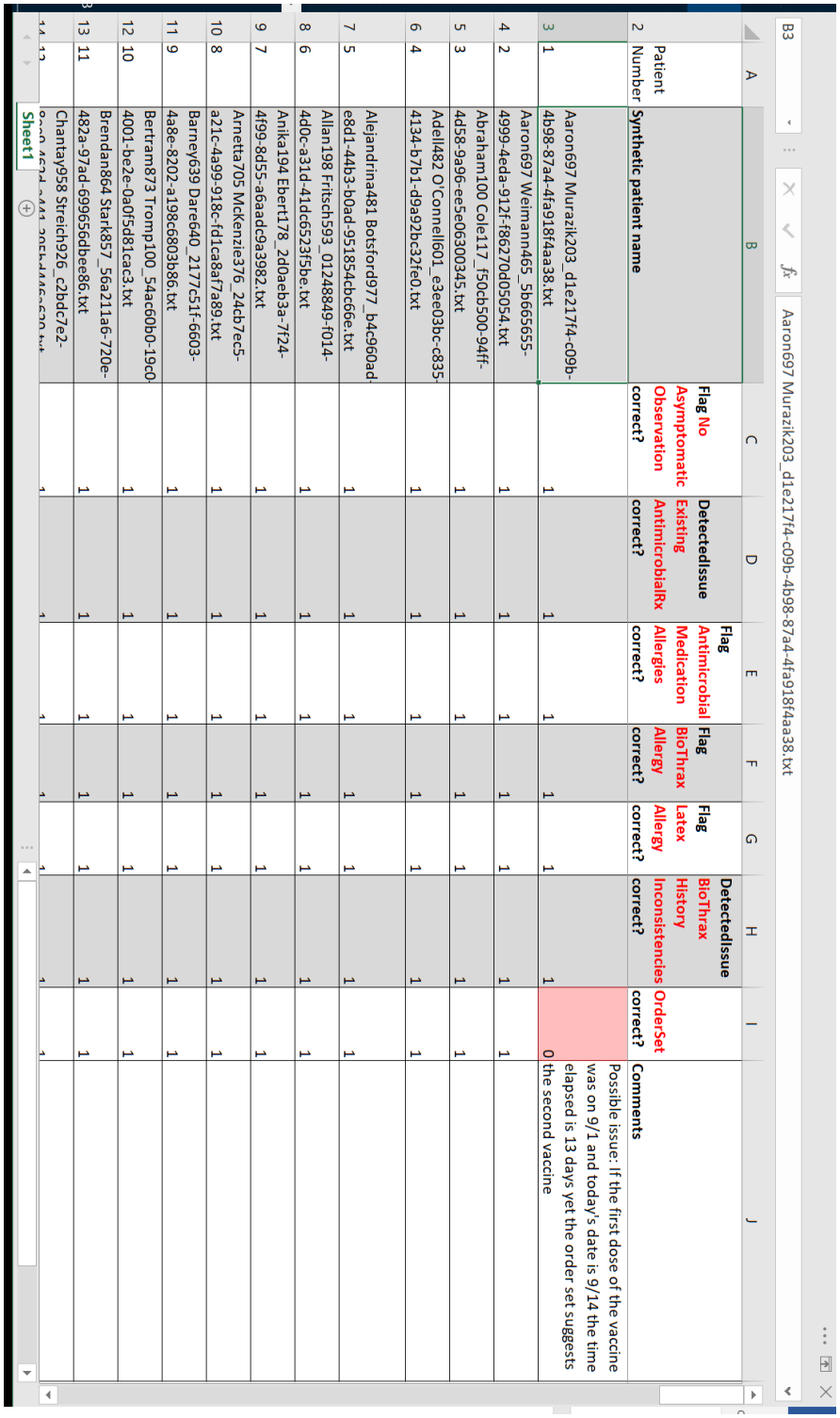
Integration Questions:

17. Is the provided documentation and Implementation Guide sufficiently clear to allow integration into your system? Yes☐ No☐
18. Which of the following provides the [most/least] benefit in terms of informing you about integrating this CDS, and why? Please rank each from 1 to 4, where 1 is most informative and 4 is the least.
    - CQL logic — Choose an item.
    - Supporting documentation files — Choose an item.
    - Metadata/semi-structured spreadsheet — Choose an item.
    - Implementation Guide — Choose an item.

    Click or tap here to enter text.
19. Is it clear what the data requirements are for this CDS? Yes☐ No☐
20. Is it clear what the data outputs of this CDS are? Yes☐ No☐
21. What types of resource and/or code mapping would your organization have to employ to integrate this CDS?
    Click or tap here to enter text.
22. What additional information is there that you feel is not included with this CDS but would be required for your organization to reliably integrate this CDS?
    Click or tap here to enter text.
23. What, if anything, would you have done differently to make the CDS easier to implement?
    Click or tap here to enter text.

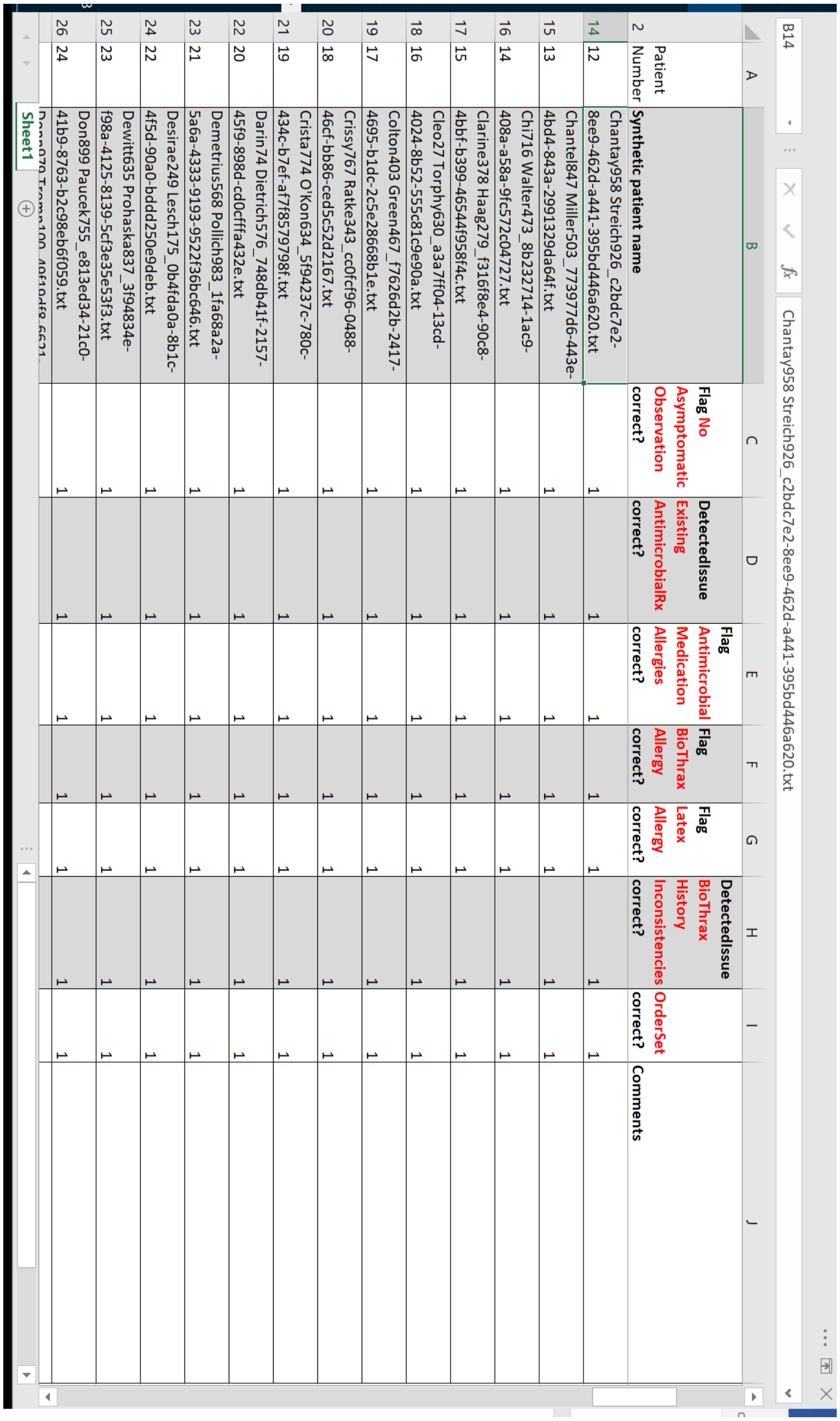
Figure 7. Anthrax CDS Artifact Evaluation Questionnaire

Appendix B. Evaluation Results



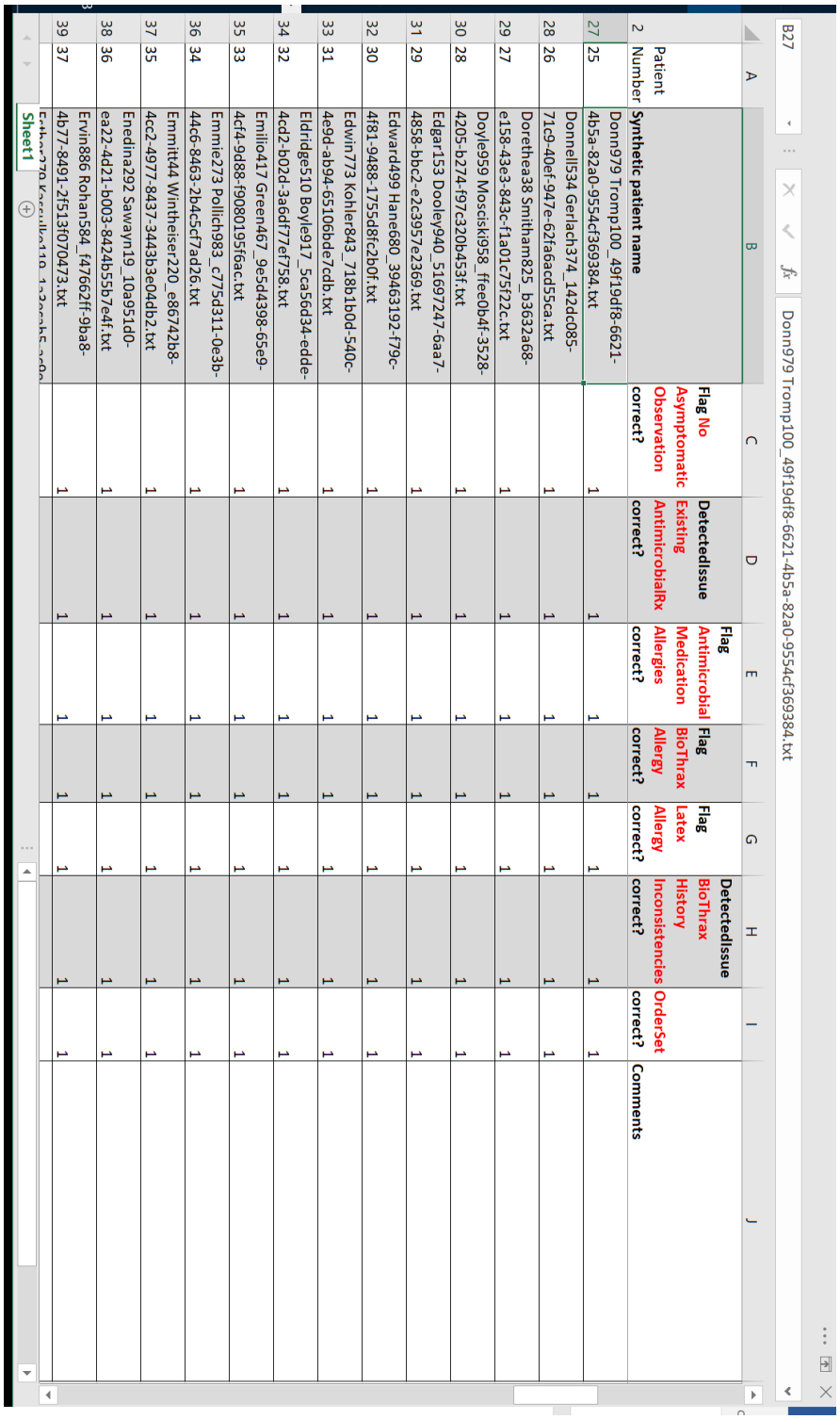
Patient Number	Synthetic patient name	Flag No Asymptomatic Observation correct?	DetectedIssue Existing Antimicrobial Rx correct?	Flag Antimicrobial Medication Allergies correct?	Flag BioThrax Allergy correct?	Flag Latex Allergy correct?	DetectedIssue BioThrax History Inconsistencies correct?	OrderSet correct?	Comments
1	Aaron697 Murazik203_d1e217f4-c09b-4b98-87a4-4fa918f4aa38.txt	1	1	1	1	1	1	0	Possible issue: If the first dose of the vaccine was on 9/1 and today's date is 9/14 the time elapsed is 13 days yet the order set suggests the second vaccine
2	Aaron697 Weimann465_5b665655-4999-4eda-912f-f86270d0504.txt	1	1	1	1	1	1	1	
3	Abraham100 Cole117_f50cb500-94ff-4d58-9a96-ee5e0630345.txt	1	1	1	1	1	1	1	
4	Adell482 O'Connell601_e3ee03bc-c835-4134-b7b1-d9a92bc32fe0.txt	1	1	1	1	1	1	1	
5	Alejandrina481 Botsford977_b4c960ad-e8d1-44b3-b0ad-951854cbc66e.txt	1	1	1	1	1	1	1	
6	Allan198 Fritsch593_01248849-f014-4d0c-a31d-41dc6523f5be.txt	1	1	1	1	1	1	1	
7	Anika194 Ebert178_2d0aeb3a-7f24-4f99-8d55-a6aadc9a3982.txt	1	1	1	1	1	1	1	
8	Arnetta705 McKenzie376_24cb7ec5-a21c-4a99-918c-fd1ca8af7a89.txt	1	1	1	1	1	1	1	
9	Barney639 Dare640_2177c51f-6603-4a8e-8202-a198c6803b86.txt	1	1	1	1	1	1	1	
10	Bertram873 Tromp100_54ac60b0-19c0-4001-be2e-0a0f5d81cac3.txt	1	1	1	1	1	1	1	
11	Brendan864 Stark857_56a211a6-720e-482a-97ad-699656dbee86.txt	1	1	1	1	1	1	1	
12	Chantay958 Streich926_c2bdc7e2-								

Figure 8. Synthetic Pilot Evaluation Results, Page 1



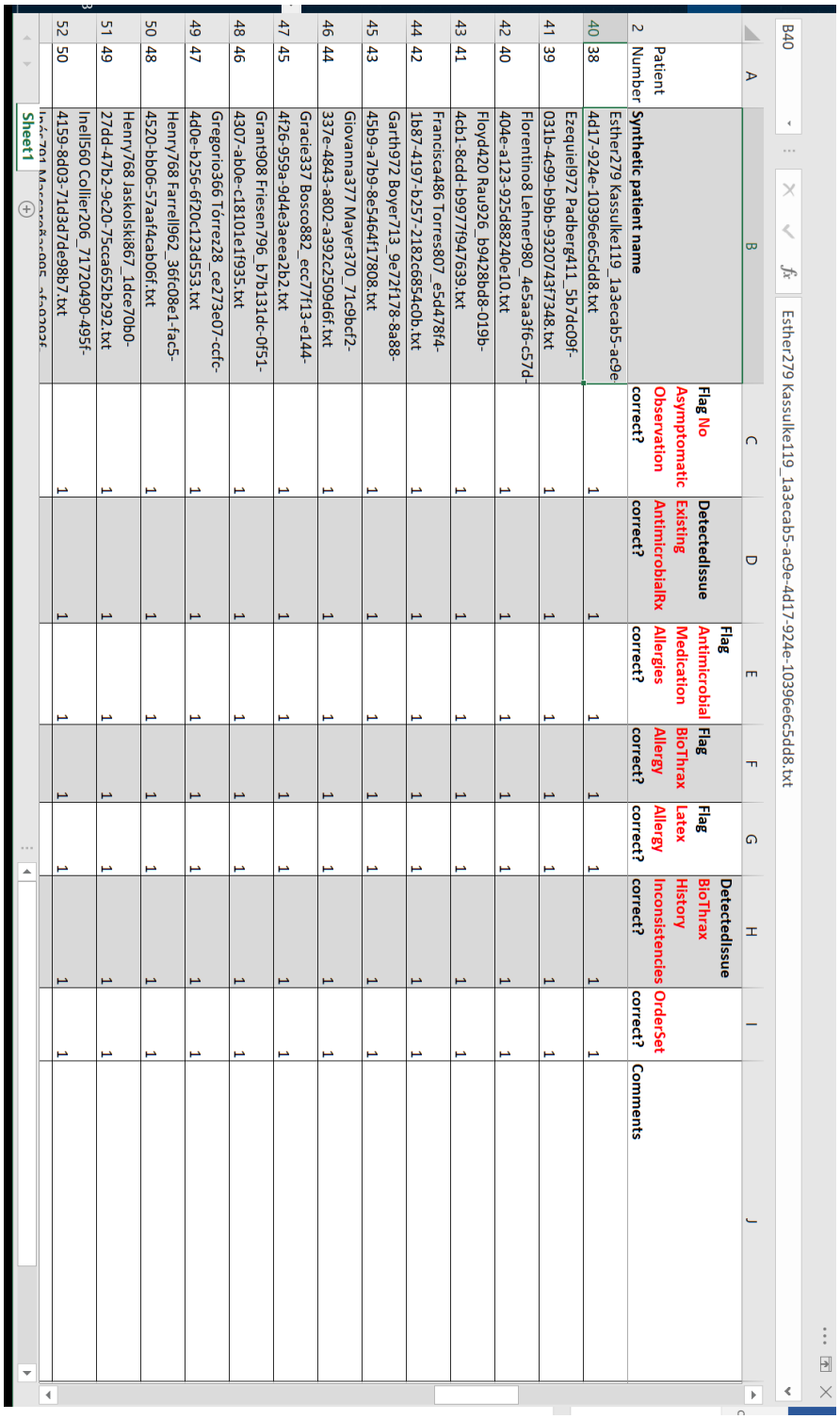
2 Patient Number	Synthetic patient name	Flag No Asymptomatic Observation correct?	DetectedIssue Existing AntimicrobialRx correct?	Flag Antimicrobial Medication Allergies correct?	Flag BioThrax Allergy correct?	Flag Latex Allergy correct?	DetectedIssue BioThrax History Inconsistencies correct?	OrderSet correct?	Comments
14 12	Chantay958 Streich926_c2bdc7e2-8ee9-462d-a441-395bd446a620.txt	1	1	1	1	1	1	1	
15 13	Chantel847 Miller503_773977d6-443e-4bd4-843a-2991329da64f.txt	1	1	1	1	1	1	1	
16 14	Chi716 Walter473_8b232714-1ac9-408a-a58a-9fc572c04727.txt	1	1	1	1	1	1	1	
17 15	Clarine378 Haag279_f316f8e4-90c8-4bbf-b399-46544f958f4c.txt	1	1	1	1	1	1	1	
18 16	Cleo27 Torphy630_a3a7ff04-13cd-4024-8b52-555c81c9e90a.txt	1	1	1	1	1	1	1	
19 17	Colton403 Green467_f7626d2b-2417-4695-b1dc-2c5e28668b1e.txt	1	1	1	1	1	1	1	
20 18	Crissy767 Ratke343_cc0fcf96-0488-46cf-bb86-ced5c52d2167.txt	1	1	1	1	1	1	1	
21 19	Crista774 O'Kon634_5f94237c-780c-434c-b7ef-af7f8579798f.txt	1	1	1	1	1	1	1	
22 20	Darin74 Dietrich576_748db41f-2157-45f9-898d-cd0cfffa432e.txt	1	1	1	1	1	1	1	
23 21	Demetrius568 Pollich983_1fa68a2a-5a6a-4333-9193-9522f36bc646.txt	1	1	1	1	1	1	1	
24 22	Desirae249 Lesch175_0b4fda0a-8b1c-4f5d-90a0-bddd250e9deb.txt	1	1	1	1	1	1	1	
25 23	Dewitt635 Prohaska837_3f94834e-f98a-4125-8139-5cf3e35e53f3.txt	1	1	1	1	1	1	1	
26 24	Don899 Paucek755_e813ed34-21c0-41b9-8763-b2c98eb6f059.txt	1	1	1	1	1	1	1	

Figure 9. Synthetic Pilot Evaluation Results, Page 2



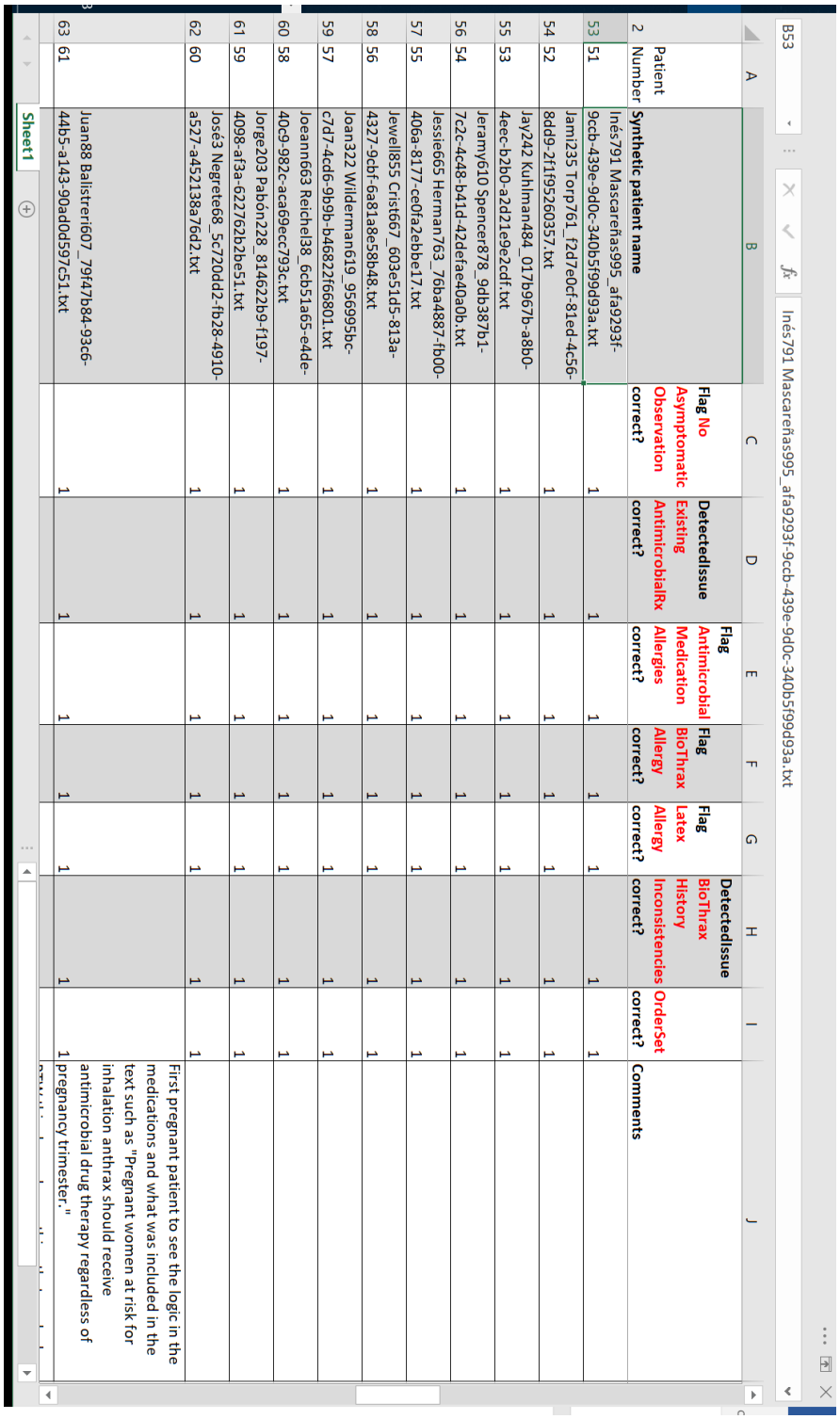
Patient Number	Synthetic patient name	Flag No Asymptomatic Observation correct?	DetectedIssue Existing Antimicrobial Rx correct?	Flag Antimicrobial Medication Allergies correct?	Flag BioThrax Allergy correct?	Flag Latex Allergy correct?	DetectedIssue BioThrax History Inconsistencies correct?	OrderSet correct?	Comments
25	Donn979 Tromp100_49f19df8-6621-4b5a-82a0-9554cf369384.txt	1	1	1	1	1	1	1	
26	Donnell534 Gerlach374_142dc085-71c9-40ef-947e-62fa6acd55ca.txt	1	1	1	1	1	1	1	
27	Dorethea38 Smitham825_b3632a68-e158-43e3-843c-f1a01c75f22c.txt	1	1	1	1	1	1	1	
28	Doyle959 Mosciski958_ffee0b4f-3528-4205-b274-f97c320b453f.txt	1	1	1	1	1	1	1	
29	Edgar153 Dooley940_51697247-6aa7-4858-bbc2-e2c3957e2369.txt	1	1	1	1	1	1	1	
30	Edward499 Hane680_39463192-f79c-4f81-9488-1755d8f62b0f.txt	1	1	1	1	1	1	1	
31	Edwin773 Kohler843_718b1b0d-540c-4e9d-ab94-65106bde7cdb.txt	1	1	1	1	1	1	1	
32	Eldridge510 Boyle917_5ca56d34-edde-4cd2-b02d-3a6df77ef758.txt	1	1	1	1	1	1	1	
33	Emilio417 Green467_9e5d4398-65e9-4cf4-9d88-f9080195f6ac.txt	1	1	1	1	1	1	1	
34	Emmie273 Pollich983_c775d311-0e3b-44c6-8463-2b4c5cf7ad26.txt	1	1	1	1	1	1	1	
35	Emmitt44 Wintheiser220_e867742b-4cc2-4977-8437-3443b3e04db2.txt	1	1	1	1	1	1	1	
36	Enedina292 Sawayn19_10a951d0-ea22-4d21-b003-8424b55b7e4f.txt	1	1	1	1	1	1	1	
37	Ervin886 Rohan584_f47662ff-9ba8-4b77-8491-2f513f070473.txt	1	1	1	1	1	1	1	

Figure 10. Synthetic Pilot Evaluation Results, Page 3



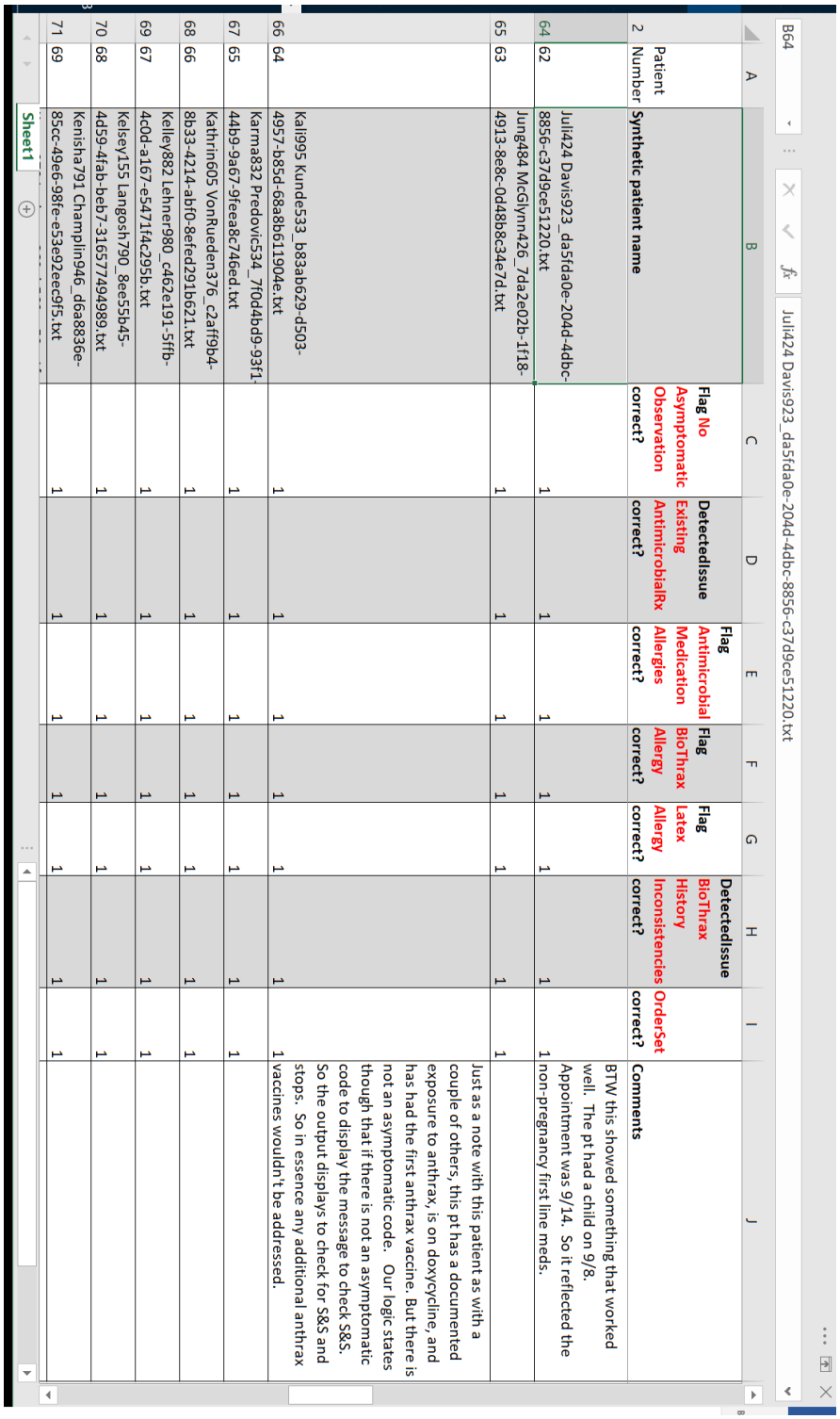
Patient Number	Synthetic patient name	Flag No Asymptomatic Observation correct?	DetectedIssue Existing Antimicrobial Rx correct?	Flag Antimicrobial Medication Allergies correct?	Flag BioThrax Allergy correct?	Flag Latex Allergy correct?	DetectedIssue BioThrax History Inconsistencies correct?	OrderSet correct?	Comments
38	Esther279 Kassulke119_1a3ecab5-ac9e-4d17-924e-10396e6c5dd8.txt	1	1	1	1	1	1	1	
39	Ezequiel972 Padberg411_5b7dc09f-031b-4c99-b9bb-93207437f348.txt	1	1	1	1	1	1	1	
40	Florentino8 Lehner980_4e5aa3f6-c57d-404e-a123-925d88240e10.txt	1	1	1	1	1	1	1	
41	Floyd420 Rau926_b9428bd8-019b-4cb1-8cdd-b9977f947639.txt	1	1	1	1	1	1	1	
42	Francisca486 Torres807_e5d47814-1b87-4197-b257-2182c6854c0b.txt	1	1	1	1	1	1	1	
43	Garth972 Boyer713_9e72f178-8a88-45b9-a7b9-8e5464f17808.txt	1	1	1	1	1	1	1	
44	Giovanna377 Mayer370_71c9bcf2-337e-4843-a802-a392c2509d6f.txt	1	1	1	1	1	1	1	
45	Gracie337 Bosco882_ecc77f13-e144-4f26-959a-9d4e3aeea2b2.txt	1	1	1	1	1	1	1	
46	Grant908 Friesen796_b7b131dc-0f51-4307-ab0e-c18101e1f935.txt	1	1	1	1	1	1	1	
47	Gregorio366 Tórrez28_ce273e07-ccfc-4d0e-b256-6f20c123d553.txt	1	1	1	1	1	1	1	
48	Henry768 Farrell962_36fc08e1-fac5-4520-bb06-57aaf4cab06f.txt	1	1	1	1	1	1	1	
49	Henry768 Jaskolski867_1dce70b0-27dd-47b2-9c20-75cca652b292.txt	1	1	1	1	1	1	1	
50	Inell560 Collier206_71720490-495f-4159-8d03-71d3d7de98b7.txt	1	1	1	1	1	1	1	

Figure 11. Synthetic Pilot Evaluation Results, Page 4



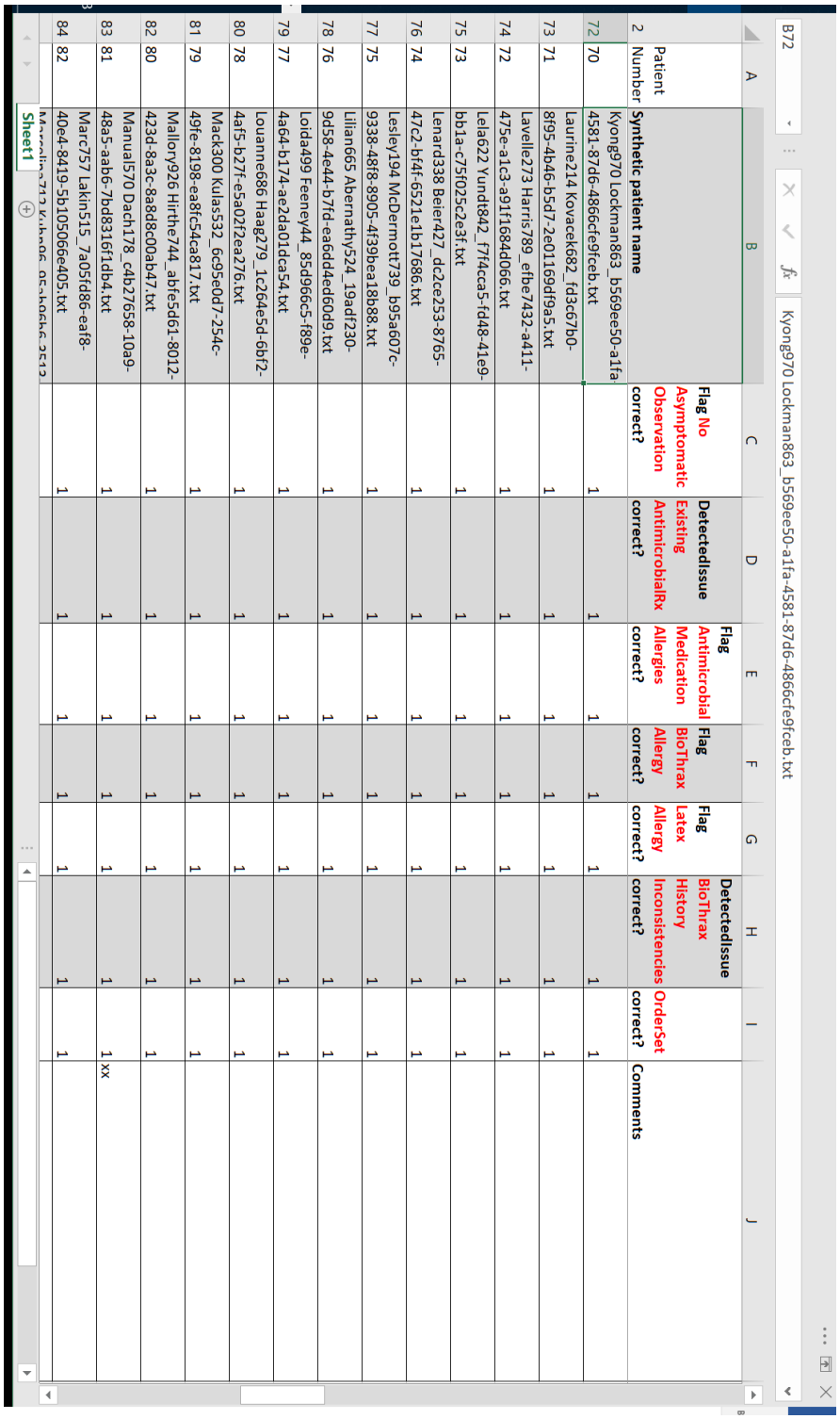
Patient Number	Synthetic patient name	Flag No Asymptomatic Observation correct?	DetectedIssue Existing Antimicrobial Rx correct?	Flag Antimicrobial Medication Allergies correct?	Flag BioThrax Allergy correct?	Flag Latex Allergy correct?	DetectedIssue BioThrax History Inconsistencies correct?	OrderSet correct?	Comments
53 51	Inés791 Mascareñas995_afa9293f-9ccb-439e-9d0c-340b5f99d93a.txt	1	1	1	1	1	1	1	
54 52	Jami235 Torp761_f2d7e0cf-81ed-4c56-8dd9-2f1f95260357.txt	1	1	1	1	1	1	1	
55 53	Jay242 Kuhlman484_017b967b-a8b0-4eec-b2b0-a2d21e9e2cdf.txt	1	1	1	1	1	1	1	
56 54	Jeramy610 Spencer878_9db387b1-7c2c-4c48-b41d-42defae40a0b.txt	1	1	1	1	1	1	1	
57 55	Jessie665 Herman763_76ba4887-fb00-406a-8177-ce0fa2ebbe17.txt	1	1	1	1	1	1	1	
58 56	Jewell855 Cristi667_603e51d5-813a-4327-9cbf-6a81a8e58b48.txt	1	1	1	1	1	1	1	
59 57	Joan322 Wilderman619_956995bc-c7d7-4cd6-9b9b-b46822f66801.txt	1	1	1	1	1	1	1	
60 58	Joeann663 Reichel38_6cb51a65-e4de-40c9-982c-aca69ecc793c.txt	1	1	1	1	1	1	1	
61 59	Jorge203 Pabón228_814622b9-f197-4098-af3a-6227626b2be51.txt	1	1	1	1	1	1	1	
62 60	José3 Negrete68_5c720dd2-fb28-4910-a527-a452138a76d2.txt	1	1	1	1	1	1	1	
63 61	Juan88 Balistreri607_79f47b84-93c6-44b5-a143-90ad0d597c51.txt	1	1	1	1	1	1	1	First pregnant patient to see the logic in the medications and what was included in the text such as "Pregnant women at risk for inhalation anthrax should receive antimicrobial drug therapy regardless of pregnancy trimester."

Figure 12. Synthetic Pilot Evaluation Results, Page 5



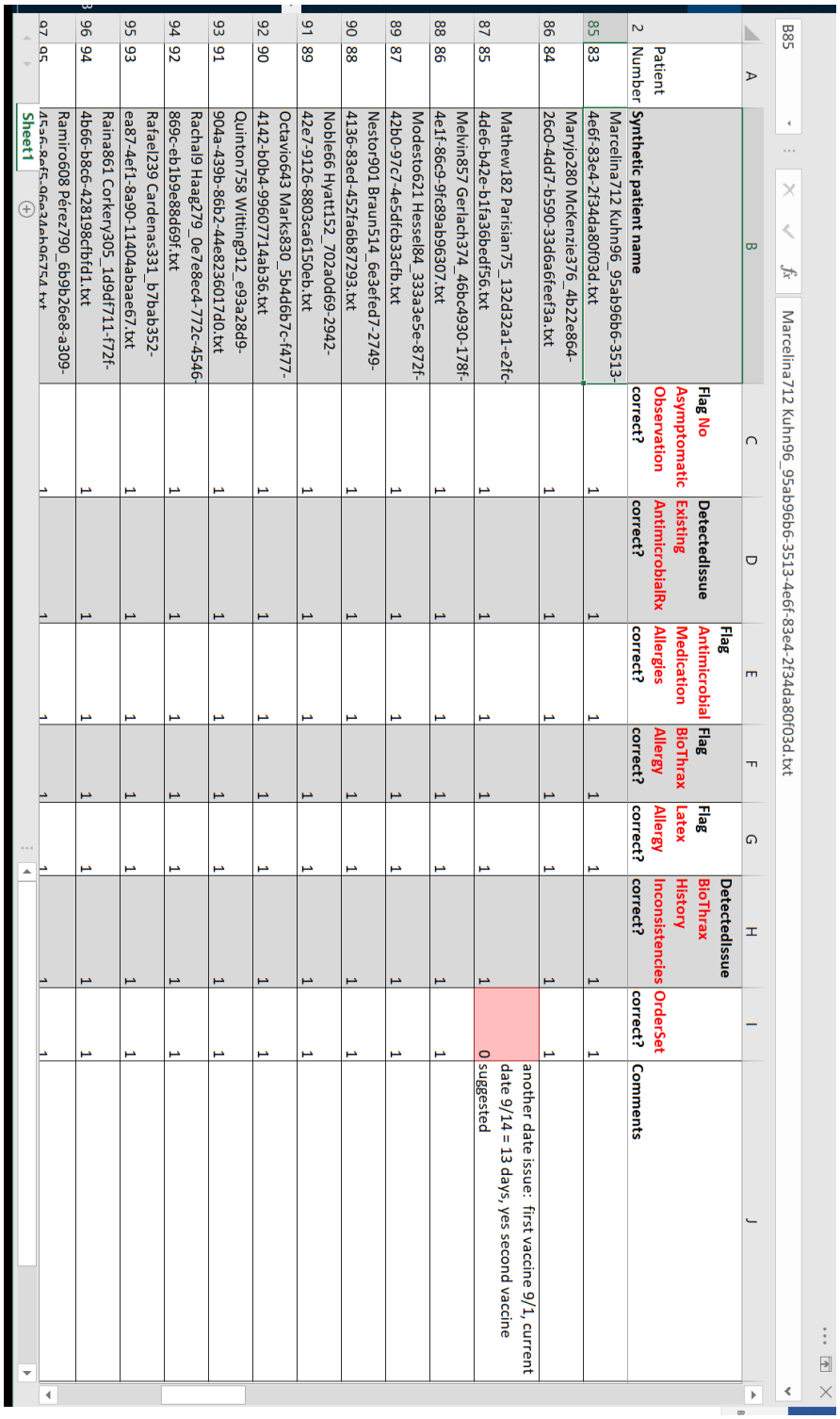
Patient Number	Synthetic patient name	Flag No Asymptomatic Observation correct?	DetectedIssue Existing AntimicrobialRx correct?	Flag Antimicrobial Medication Allergies correct?	Flag BioThrax Allergy correct?	Flag Latex Allergy correct?	DetectedIssue BioThrax History Inconsistencies correct?	OrderSet correct?	Comments
62	Juli424 Davis923_da5fda0e-204d-4dbc-8856-c37d9ce51220.txt	1	1	1	1	1	1	1	BTW this showed something that worked well. The pt had a child on 9/8. Appointment was 9/14. So it reflected the non-pregnancy first line meds.
63	Jung484 McGlynn426_7da2e02b-1f18-4913-8e8c-0d48b8c34e7d.txt	1	1	1	1	1	1	1	
64	Kali995 Kunde533_b83ab629-d503-4957-b85d-68a8b611904e.txt	1	1	1	1	1	1	1	Just as a note with this patient as with a couple of others, this pt has a documented exposure to anthrax, is on doxycycline, and has had the first anthrax vaccine. But there is not an asymptomatic code. Our logic states though that if there is not an asymptomatic code to display the message to check S&S. So the output displays to check for S&S and stops. So in essence any additional anthrax vaccines wouldn't be addressed.
65	Karma832 Predovic534_7f0d4bd9-93f1-44b9-9a67-9feea8c746ed.txt	1	1	1	1	1	1	1	
66	Kathrin605 VonRueden376_c2aff9b4-8b33-4214-abf0-8efed291b621.txt	1	1	1	1	1	1	1	
67	Kelley882 Lehner980_c462e191-5ffb-4c0d-a167-e5471f4c295b.txt	1	1	1	1	1	1	1	
68	Kelsey155 Langosh790_8ee55b45-4d59-4fab-beb7-31657749989.txt	1	1	1	1	1	1	1	
69	Kenisha791 Champlin946_d6a8836e-85cc-49e6-98fe-e53e92eec9f5.txt	1	1	1	1	1	1	1	

Figure 13. Synthetic Pilot Evaluation Results, Page 6



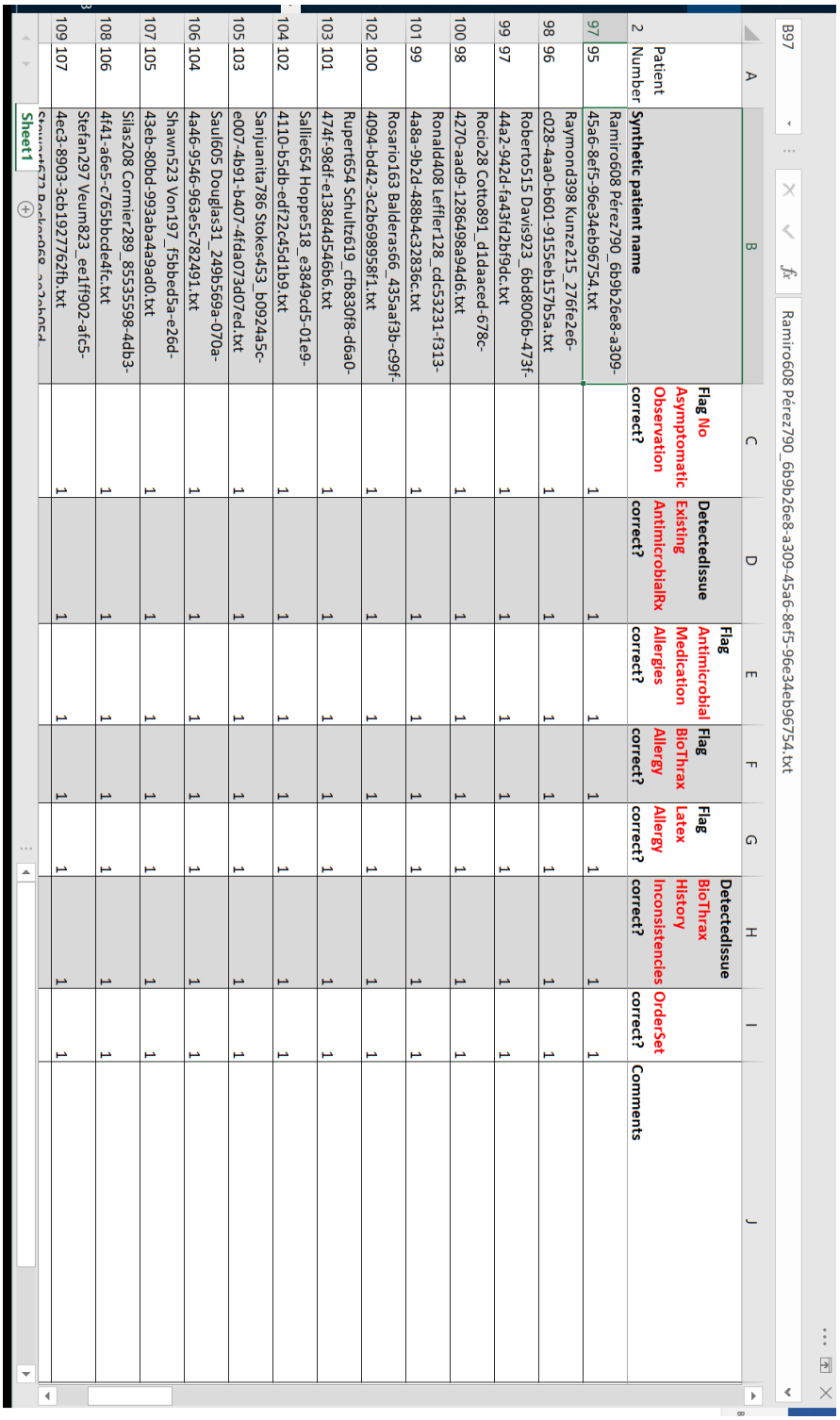
Patient Number	Synthetic patient name	Flag No Asymptomatic Observation correct?	DetectedIssue Existing Antimicrobial Rx correct?	Flag Antimicrobial Medication Allergies correct?	Flag BioThrax Allergy correct?	Flag Latex Allergy correct?	DetectedIssue BioThrax History Inconsistencies correct?	OrderSet correct?	Comments
70	Kyong970 Lockman863_b569ee50-a1fa-4581-87d6-4866cfe9fceb.txt	1	1	1	1	1	1	1	
71	Laurine214 Kovacek682_fd3c67b0-8f95-4b46-b5d7-2e01169df9a5.txt	1	1	1	1	1	1	1	
72	Lavelle273 Harris789_efbe7432-a411-475e-a1c3-a91f1684d066.txt	1	1	1	1	1	1	1	
73	Lela622 Yundt842_f7f4cca5-fd48-41e9-bb1a-c75f025c2e3f.txt	1	1	1	1	1	1	1	
74	Lenard338 Beier427_dc2ce253-8765-47c2-bf4f-6521e1b17686.txt	1	1	1	1	1	1	1	
75	Lesley194 McDermott739_b95a607c-9338-48f8-8905-4f39bea18b88.txt	1	1	1	1	1	1	1	
76	Lilian665 Abernathy524_19adf230-9d58-4e44-b7fd-ea6dd4ed60d9.txt	1	1	1	1	1	1	1	
77	Loida499 Feeney44_85d966c5-f89e-4a6d-b174-ae2da01dca54.txt	1	1	1	1	1	1	1	
78	Louanne686 Haag279_1c264e5d-6bf2-4af5-b27f-e5a02f2ea276.txt	1	1	1	1	1	1	1	
79	Mack300 Kulas532_6c95e0d7-254c-49fe-8198-ea8fc54ca817.txt	1	1	1	1	1	1	1	
80	Mallory926 Hirthe744_abfe5d61-8012-423d-8a3c-8a8d8c00ab47.txt	1	1	1	1	1	1	1	
81	Manual570 Dach178_c4b27658-10a9-48a5-aab6-7bd8316f1db4.txt	1	1	1	1	1	1	1	xx
82	Marc757 Lakin515_7a05fd86-eaf8-40e4-8419-5b105066e405.txt	1	1	1	1	1	1	1	

Figure 14. Synthetic Pilot Evaluation Results, Page 7



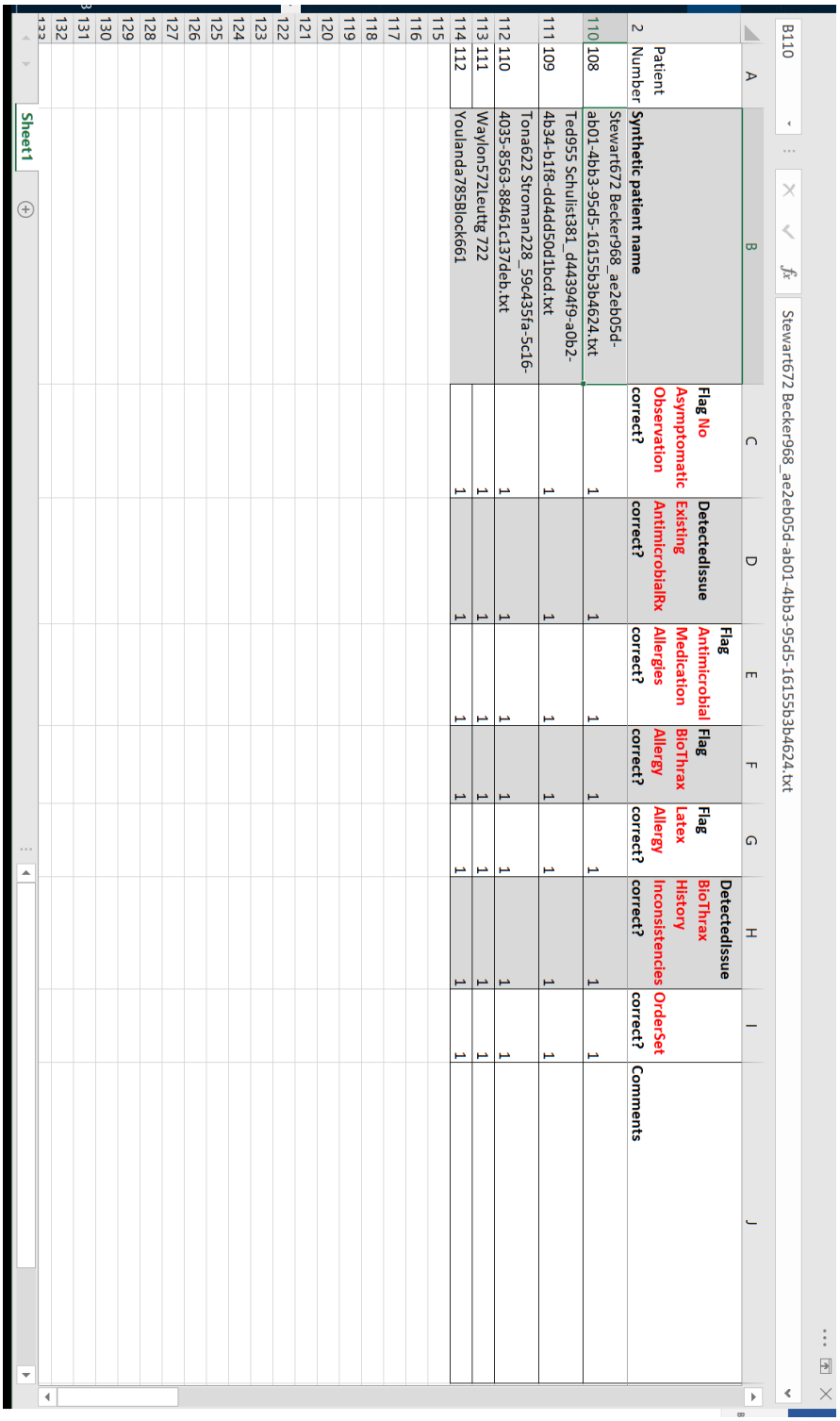
Patient Number	Synthetic patient name	Flag No Asymptomatic Observation correct?	DetectedIssue Existing AntimicrobialRx correct?	Flag Antimicrobial Medication Allergies correct?	Flag BioThrax Allergy correct?	Flag Latex Allergy correct?	DetectedIssue BioThrax History Inconsistencies correct?	OrderSet correct?	Comments
83	Marcelina712 Kuhn96_95ab96b6-3513-4e6f-83e4-2f34da80f03d.txt	1	1	1	1	1	1	1	
84	Manyjo280 McKenzie376_4b22e864-26c0-4dd7-b590-33d6a6feef3a.txt	1	1	1	1	1	1	1	
85	Mathew182 Parisian75_132d32a1-e2fc-4de6-b42e-b1fa36bedf56.txt	1	1	1	1	1	1	0	another date issue: first vaccine 9/1, current date 9/14 = 13 days, yes second vaccine suggested
86	Melvin857 Gerlach374_46bc4930-178f-4e1f-86c9-9fc89ab96307.txt	1	1	1	1	1	1	1	
87	Modesto621 Hessel84_333a3e5e-872f-42b0-97c7-4e5dfcb33cfb.txt	1	1	1	1	1	1	1	
88	Nestor901 Braun514_6e3efed7-2749-4136-83ed-452fa6b87293.txt	1	1	1	1	1	1	1	
89	Noble66 Hyatt152_702a0d69-2942-42e7-9126-8803ca6150eb.txt	1	1	1	1	1	1	1	
90	Octavio643 Marks830_5b4d6b7c-f477-4142-b0b4-99607714ab36.txt	1	1	1	1	1	1	1	
91	Quinton758 Witting912_e93a28d9-904a-439b-86b2-44e8236017d0.txt	1	1	1	1	1	1	1	
92	Rachal9 Haag279_0e7e8ec4-772c-4546-869c-eb1b9e88d69f.txt	1	1	1	1	1	1	1	
93	Rafael239 Cardenas331_b7bab352-ea87-4ef1-8a90-11404abaae67.txt	1	1	1	1	1	1	1	
94	Raina861 Corkery305_1d9d7711-f72f-4b66-b8c6-428198cfbfd1.txt	1	1	1	1	1	1	1	
95	Ramiro608 Pérez790_6b9b26e8-a309-45e6-8ef5-9fe24fab9675.txt	1	1	1	1	1	1	1	

Figure 15. Synthetic Pilot Evaluation Results, Page 8



Patient Number	Synthetic patient name	Flag No Asymptomatic Observation correct?	DetectedIssue Existing AntimicrobialRx correct?	Flag Antimicrobial Medication Allergies correct?	Flag BioThrax Allergy correct?	Flag Latex Allergy correct?	DetectedIssue BioThrax History Inconsistencies correct?	OrderSet correct?	Comments
95	Ramiro608 Pérez790_6b9b26e8-a309-45a6-8ef5-96e34eb96754.txt	1	1	1	1	1	1	1	
96	Raymond398 Kunze215_276fe2e6-c028-4aa0-b601-9155eb157b5a.txt	1	1	1	1	1	1	1	
97	Roberto515 Davis923_6bd8006b-473f-44a2-942d-fa43fd2bf9dc.txt	1	1	1	1	1	1	1	
98	Rocio28 Cotto891_d1daaced-678c-4270-aad9-1286498a94d6.txt	1	1	1	1	1	1	1	
99	Ronald408 Leffler128_cdc53231-f313-4a8a-9b2d-488b4c32836c.txt	1	1	1	1	1	1	1	
100	Rosario163 Balderas66_435aaf3b-c99f-4094-bd42-3c2b698958f1.txt	1	1	1	1	1	1	1	
101	Rupert654 Schultz619_cfb830f8-d6a0-474f-98df-e138d4d546b6.txt	1	1	1	1	1	1	1	
102	Sallie654 Hoppe518_e3849cd5-01e9-4110-b5db-edf22c45d1b9.txt	1	1	1	1	1	1	1	
103	Sanjuanita786 Stokes453_b0924a5c-e007-4b91-b407-4fda073d07ed.txt	1	1	1	1	1	1	1	
104	Saul605 Douglas31_249b569a-070a-4a46-9546-963e5c782491.txt	1	1	1	1	1	1	1	
105	Shawn523 Von197_f5bbed5a-e26d-43eb-80bd-993aba4a9ad0.txt	1	1	1	1	1	1	1	
106	Silas208 Cormier289_85535598-4db3-4f41-a6e5-c765bbcde4fc.txt	1	1	1	1	1	1	1	
107	Stefan297 Veum823_ee1ff902-afc5-4ec3-8903-3cb1927762fb.txt	1	1	1	1	1	1	1	

Figure 16. Synthetic Pilot Evaluation Results, Page 9



Patient Number	Synthetic patient name	Flag No Asymptomatic Observation correct?	DetectedIssue Existing Antimicrobial Rx correct?	Flag Antimicrobial Medication Allergies correct?	Flag BioThrax Allergy correct?	Flag Latex Allergy correct?	DetectedIssue BioThrax History Inconsistencies correct?	OrderSet correct?	Comments
108	Stewart672 Becker968_ae2eb05d-ab01-4bb3-95d5-16155b3b4624.txt		1	1	1	1	1	1	
109	Ted955 Schulist381_d4439f49-a0b2-4b34-b1f8-dd4dd50d1bcd.txt	1	1	1	1	1	1	1	
110	Tona622 Stroman228_59c435fa-5c16-4035-8563-88461c137deb.txt	1	1	1	1	1	1	1	
111	Waylon572Leuttg722	1	1	1	1	1	1	1	
112	Youlanda785Block661	1	1	1	1	1	1	1	

Figure 17. Synthetic Pilot Evaluation Results, Page 10

Acronyms

CAMH	CMS Alliance to Modernize Healthcare
CDC	Centers for Disease Control and Prevention
CDS	Clinical Decision Support
CQL	Clinical Quality Language
CQM	Clinical Quality Measures
DSTU	Draft Standard for Trial Use
EHR	Electronic Health Record
FHIR	Fast Healthcare Interoperability Resources
FFRDC	Federally Funded Research and Development Center
GMF	Generic Modeling Framework
HHS	Department of Health and Human Services
HL7	Health Level 7
JSON	JavaScript Object Notation
LOINC	Logical Observation Identifiers Names and Codes
ONC	Office of the National Coordinator for Health Information Technology
PEP	Post-Exposure Prophylaxis
SME	Subject Matter Expert
STU	Standard for Trial Use
TDD	Test-Driven Development

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